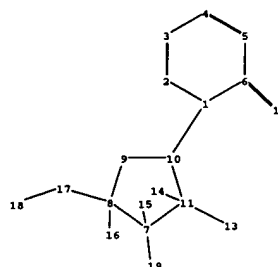
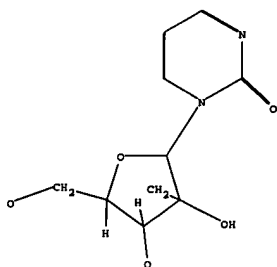


10/609,298



chain nodes :

12 13 14 15 16 17 18 19

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :

1-10 6-12 7-15 7-19 8-16 8-17 11-13 11-14 17-18

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11

exact/norm bonds :

1-2 1-6 1-10 2-3 3-4 4-5 5-6 6-12 7-8 7-11 7-19 8-9 9-10 10-11 11-13

exact bonds :

7-15 8-16 8-17 11-14 17-18

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:CLASS  
 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS

10/609,298

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NEWS 7 MAY 19 Derwent World Patents Index to be reloaded and enhanced  
NEWS 8 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAPLUS and  
USPATFULL/USPAT2  
NEWS 9 MAY 30 The F-Term thesaurus is now available in CA/CAPLUS  
NEWS 10 JUN 02 The first reclassification of IPC codes now complete in  
INPADOC  
NEWS 11 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and  
and display fields  
NEWS 12 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL  
NEWS 13 JUL 07 Coverage of Research Disclosure reinstated in DWPI  
  
NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.  
  
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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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0.21

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10/609,298

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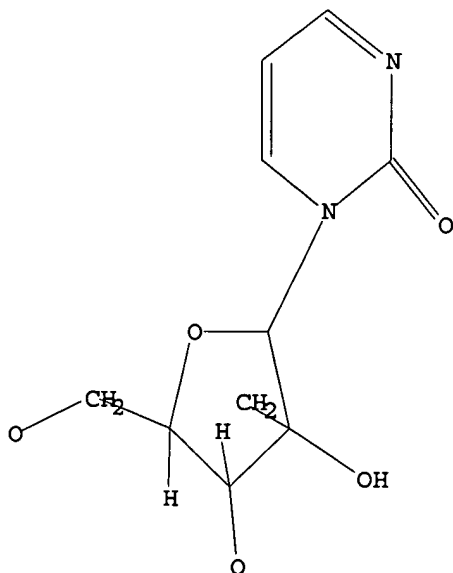
Uploading C:\Program Files\Stnexp\Queries\10609298.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 13:35:34 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED

12 ITERATIONS

6 ANSWERS

10/609,298

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 33 TO 447  
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

=> s l1 full  
FULL SEARCH INITIATED 13:35:38 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 296 TO ITERATE

100.0% PROCESSED 296 ITERATIONS 142 ANSWERS  
SEARCH TIME: 00.00.01

L3 142 SEA SSS FUL L1

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FULL ESTIMATED COST 166.94 167.15

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FILE COVERS 1907 - 10 Jul 2006 VOL 145 ISS 3  
FILE LAST UPDATED: 9 Jul 2006 (20060709/ED)

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=> s l3 and hepatitis  
68 L3  
53791 HEPATITIS  
L4 16 L3 AND HEPATITIS

=> s l3 and flaviviridae  
68 L3  
452 FLAVIVIRIDAE  
L5 8 L3 AND FLAVIVIRIDAE

=> s l3 and flavivirus  
68 L3  
1371 FLAVIVIRUS  
687 FLAVIVIRUSES  
1599 FLAVIVIRUS

## (FLAVIVIRUS OR FLAVIVIRUSES)

L6 4 L3 AND FLAVIVIRUS

=&gt; s l3 and (hcv or hbv)

68 L3  
10866 HCV  
20 HCVS  
10870 HCV  
(HCV OR HCVS)  
9114 HBV  
61 HBVS  
9130 HBV  
(HBV OR HBVS)

L7 17 L3 AND (HCV OR HBV)

=&gt; s l4 or l5 or l6 or l7

L8 23 L4 OR L5 OR L6 OR L7

=&gt; d bib abs hitstr 1-23 l8

L8 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:425398 CAPLUS

DN 145:39734

TI Nucleoside analog inhibitors of hepatitis C virus replication

AU Carroll, S. S.; Olsen, D. B.

CS Department of Antiviral Research, Merck Research Laboratories, West Point, PA, 19486, USA

SO Infectious Disorders: Drug Targets (2006), 6(1), 17-29

CODEN: IDDTAD; ISSN: 1871-5265

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. Of the 30 compds. currently marketed in the United States for treatment of viral infections, 15 are nucleoside analogs, demonstrating the utility of this class of compound as a source of antiviral drugs. The success of nucleoside analogs in treating other viral infections provides a compelling rationale for the significant effort that is currently being devoted to the discovery and development of nucleoside analogs to treat infection by hepatitis C virus (HCV) that may lead to improvements in response rates compared to currently available therapies. Several different approaches were adopted to identify promising analogs, including the use of surrogate viruses in cell culture assays, screening in the cell-based bicistronic HCV replicon assay, and screening nucleoside triphosphates for the ability to inhibit the activity of the HCV RNA-dependent RNA polymerase in vitro. Several classes of ribonucleoside analogs with modifications of the ribose inhibit HCV replication. Nucleoside analogs incorporating a 2'-C-Me modification are potent inhibitors in the replicon assay in the absence of cytotoxicity, and appear to exert their inhibition by acting as functional chain terminators of RNA synthesis. NM283, a prodrug of 2'-C-methylcytidine, has entered clin. trials and demonstrated viral load redns. in subjects infected with genotype 1 HCV, a genotype known to be difficult to treat effectively with currently approved therapies. Overall, results to date offer encouragement that improved therapies to treat HCV infection including newly developed nucleoside analogs may become available within the next few years.

IT 640725-71-9, NM/283

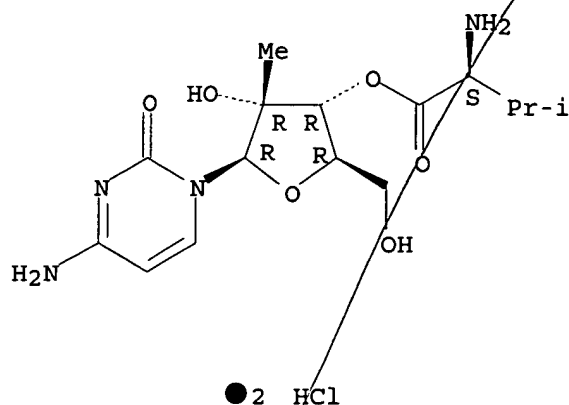
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nucleoside analog inhibitors of hepatitis C virus  
replication)

RN 640725-71-9 CAPLUS

10/609,298

CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:342840 CAPLUS

DN 144:381956

TI Combination antiviral compositions comprising castanospermine and use for the treatment and prevention of infections caused by or associated with a virus of the Flaviviridae family

IN Dugourd, Dominique

PA Migenix Inc., Can.

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006037227	A1	20060413	WO 2005-CA1528	20051006
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2006093577	A1	20060504	US 2005-244811	20051006

PRAI US 2004-616787P P 20041006

AB The invention discloses the use of castanospermine in combination with another therapeutic agent to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV), and to the use of such compds. to examine the biol. mechanisms of HCV infection.

IT 882489-96-5

RL: BSU (Biological study, unclassified); BIOL (Biological study)

10/609,298

(castanospermine-containing combination antiviral compns., and use for treatment of Flaviviridae infections)

RN 882489-96-5 CAPLUS

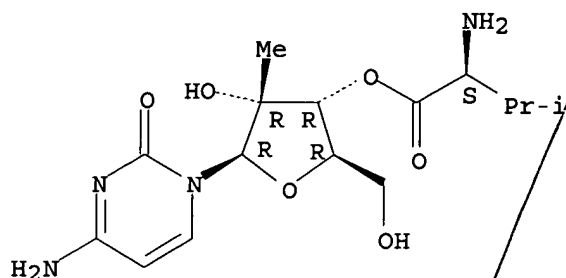
CN L-Valine, 3'-ester with 2'-C-methylcytidine, mixt. with (1S,6S,7R,8R,8aR)-octahydro-1,6,7,8-indolizinetetrol (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

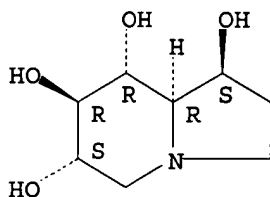


CM 2

CRN 79831-76-8

CMF C8 H15 N O4

Absolute stereochemistry. Rotation (+).



IT 640281-90-9, Valopicitabine

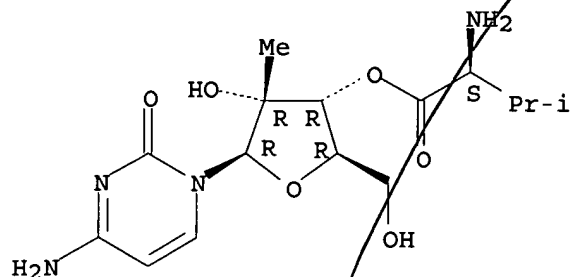
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(castanospermine-containing combination antiviral compns., and use for treatment of Flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

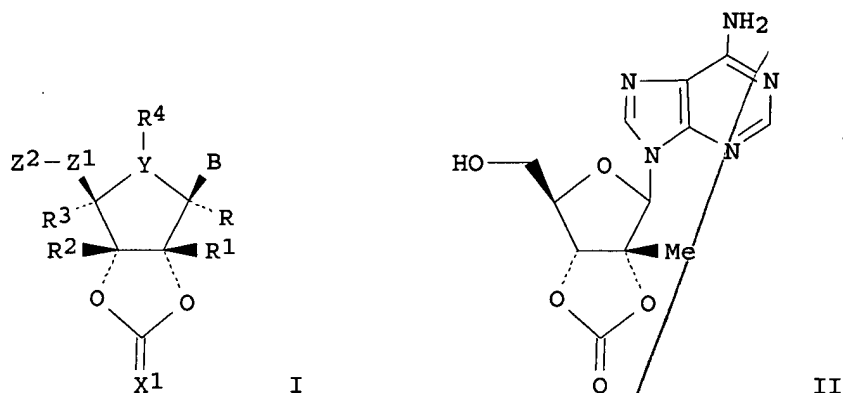


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2006:296019 CAPLUS  
DN 144:312290  
TI Preparation of nucleoside derivatives as antiviral, antitumor, and  
antidiabetic prodrug agents  
IN Reddy, Raja K.; Erion, Mark D.  
PA Metabasis Therapeutics, Inc., USA  
SO PCT Int. Appl., 255 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006033709	A2	20060330	WO 2005-US27235	20050729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2005182252	A1	20050818	US 2004-903215	20040729
PRAI US 2004-903215	A	20040729		
US 2005-652527P	P	20050211		
US 2004-544743P	P	20040213		
OS MARPAT 144:312290				
GI				





AB Nucleoside derivs. I, wherein X1 is O, S, SO, substituted nitrogen; B is heterocycle, nucleobase; Y is O, S, N, substituted C, CH2; R and R1 are independently H, alkyl, alkenyl, alkynyl, R2 is H, alkyl, alkenyl, alkynyl, alkylamino, cycloalkyl-amino, halogen, alkoxy; R3 is H, halogen, alkyl, alkoxy, alkenyl-oxy, alkylthio, alkylcarbonyl-oxy, aryloxy-carbonyl, azido, amino, alkylamino; R4 is H, alkyl, alkenyl, alkynyl, OH, alkoxy, halogen, CN, were prepared and tested in vitro and in rats for the treatment of viral diseases including hepatitis C viral infection, cancer, diabetes, and other diseases. The activation of prodrug analogs to NMP was evaluated in the microsomal fraction of human liver. The HepDirect-carbonate prodrugs evaluated were activated to the corresponding NMP in human liver microsomes, indicating that the enzymes required for removal of both the HepDirect and the carbonate prodrug moieties are present in this reaction system. Thus, nucleoside II was prepared via coupling and hydrogen transfer reactions and tested in vitro and in rats as antiviral, antitumor, and antidiabetic prodrug agents. The oral bioavailability (OBAV) of the free nucleoside is very low (<5 %) whereas the OBAV of its carbonate prodrugs are >20 %. The compds. of the present invention may also be administered in combination with an agent that is an inhibitor of HCV NS3 serine protease.

IT 879494-56-1P 879494-58-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. via coupling and hydrogen transfer reactions as antiviral, antitumor, and antidiabetic prodrug agents)

RN 879494-56-1 CAPIUS

CN Cytidine, 2'-C-methyl-5'-O-[(2R,4S)-2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

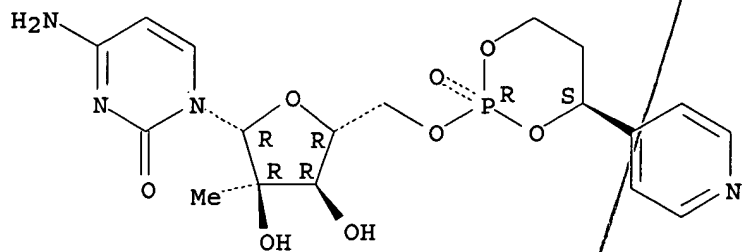
CM 1

CRN 879494-55-0

CMF C18 H23 N4 O8 P

Absolute stereochemistry.

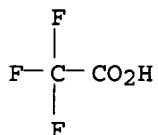
10/609,298



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 879494-58-3 CAPLUS

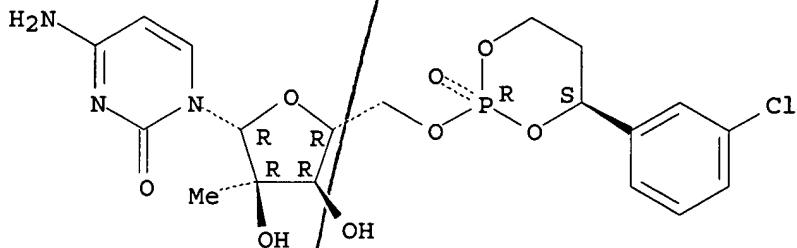
CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, trifluoroacetate (10:3) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 879494-57-2

CMF C19 H23 Cl N3 O8 P

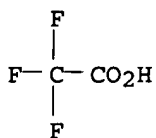
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



10/609,298

L8 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:149315 CAPLUS

DN 144:205728

TI Methods using a Type II interferon receptor agonist alone or in combination with a direct antiviral drug for treating hepatitis C virus infection

IN Blatt, Lawrence M.

PA Intermune, Inc., USA

SO PCT Int. Appl., 139 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006016930	A2	20060216	WO 2005-US16927	20050513
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRAI US 2004-571322P P 20040514

AB The invention provides methods for treating hepatitis C virus (HCV) infection; methods for reducing the incidence of complications associated with HCV and cirrhosis of the liver; and methods for reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from HCV infection. The methods generally involve administering to the individual a Type II interferon receptor agonist alone or in combination with a direct antiviral drug.

IT 640725-71-9, NM 283

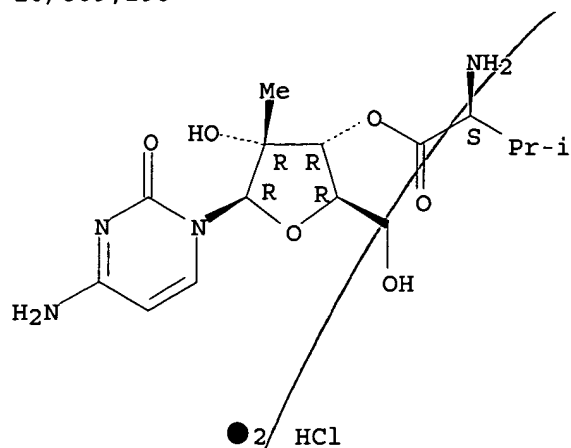
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(type II interferon receptor agonist alone or in combination with direct antiviral drug for treating hepatitis C virus infection)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:136728 CAPLUS

DN 144:324202

TI The Novel Nucleoside Analog R1479 (4'-Azidocytidine) Is a Potent Inhibitor of NS5B-dependent RNA Synthesis and Hepatitis C Virus Replication in Cell Culture

AU Klumpp, Klaus; Leveque, Vincent; Le Pogam, Sophie; Ma, Han; Jiang, Wen-Rong; Kang, Hyunsoon; Granycome, Caroline; Singer, Margaret; Laxton, Carl; Hang, Julie Qi; Sarma, Keshab; Smith, David B.; Heindl, Dieter; Hobbs, Chris J.; Merrett, John H.; Symons, Julian; Cammack, Nick; Martin, Joseph A.; Devos, Rene; Najera, Isabel

CS Roche Palo Alto LLC, Palo Alto, CA, 94304, USA

SO Journal of Biological Chemistry (2006), 281(7), 3793-3799  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Hepatitis C virus (HCV) polymerase activity is essential for HCV replication. Targeted screening of nucleoside analogs identified R1479 (4'-azidocytidine) as a specific inhibitor of HCV replication in the HCV subgenomic replicon system (IC<sub>50</sub> = 1.28 μM) with similar potency compared with 2'-C-methylcytidine (IC<sub>50</sub> = 1.13 μM). R1479 showed no effect on cell viability or proliferation of HCV replicon or Huh-7 cells at concns. up to 2 mM. HCV replicon RNA could be fully cleared from replicon cells after prolonged incubation with R1479. The corresponding 5'-triphosphate derivative (R1479-TP) is a potent inhibitor of native HCV replicase isolated from replicon cells and of recombinant HCV polymerase (NS5B)-mediated RNA synthesis activity. R1479-TP inhibited RNA synthesis as a CTP-competitive inhibitor with a K<sub>i</sub> of 40 nM. On an HCV RNA-derived template substrate (complementary internal ribosome entry site), R1479-TP showed similar potency of NS5B inhibition compared with 3'-dCTP. R1479-TP was incorporated into nascent RNA by HCV polymerase and reduced further elongation with similar efficiency compared with 3'-dCTP under the reaction conditions. The S282T point mutation in the coding sequence of NS5B confers resistance to inhibition by 2'-C-MeATP and other 2'-methyl-nucleotides. In contrast, the S282T mutation did not confer cross-resistance to R1479.

IT 20724-73-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

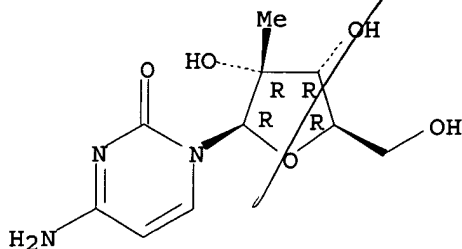
(novel nucleoside analog R1479 (4'-azidocytidine) is a potent inhibitor of NS5B-dependent RNA synthesis and hepatitis C virus replication in cell culture)

RN 20724-73-6 CAPLUS

10/609,298

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2006:103884 CAPLUS  
DN 144:171198  
TI Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl  
pyrimidine and purine nucleoside analogs via condensation of the lactone  
to nucleosides as potential antiviral agents  
IN Wang, Peiyuan; Stec, Wojciech; Clark, Jeremy; Chun, Byoung-Kwon; Shi,  
Junxing; Du, Jinfa  
PA Pharmasset, Inc., USA  
SO PCT Int. Appl., 34 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006012440	A2	20060202	WO 2005-US25916	20050721
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2005277598	A1	20051215	US 2005-118613	20050429
PRAI	US 2004-589866P	P	20040721		
	US 2004-608320P	P	20040909		
	US 2004-566584P	P	20040429		
OS	MARPAT 144:171198				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH3, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl,

3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butyldiphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thioether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3'-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N3, (un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an anti-HCV agent.

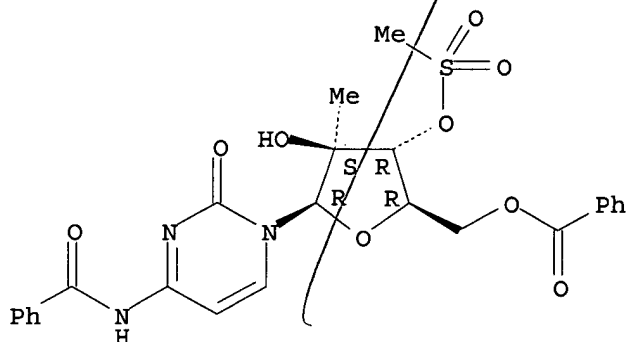
IT 874638-81-0P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)

RN 874638-81-0 CAPLUS

CN Benzamide, N-[1-[5-O-benzoyl-2-C-methyl-3-O-(methylsulfonyl)-β-D-arabinofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:684531 CAPLUS

DN 143:431740

TI Emerging drugs for chronic hepatitis C

AU Bhopale, Girish Mahadeorao; Nanda, Rabindra Kumar

CS Research and Development Division, Hindustan Antibiotics Limited, Pimpri, Pune, 411018, India

SO Hepatology Research (2005), 32(3), 146-153

CODEN: HPRSFM; ISSN: 1386-6346

PB Elsevier B.V.

DT Journal; General Review

LA English

AB A review. Hepatitis C virus (HCV) is a major cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. A combination therapy comprising pegylated interferon and ribavirin currently represents the most effective therapy for chronic HCV infection. The limitations of this current therapy mainly its

efficacy and significant side effects have prompted the development of new drugs. Few categories of therapeutic agents appear promising for future therapy, e.g. novel interferons, ribavirin analogs, antisense oligonucleotides, short interfering RNAs, ribozymes, enzyme inhibitors, immunomodulatory agents, antifibrotic agents, therapeutic vaccines and antibodies. Few drugs belong to afore-mentioned categories have already reached the different clin. phases of development. The present article highlights the status of current available therapies and emerging drugs for the treatment of hepatitis C.

IT 640725-71-9, NM 283

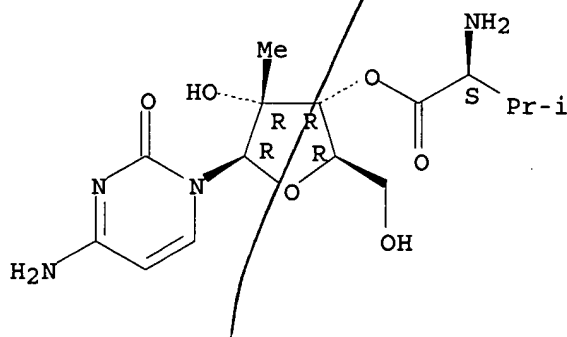
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NM283 proved promising therapeutic effect in treating chronic hepatitis C patient)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2006 ACS on STM

AN 2005:648160 CAPLUS

DN 143:248607

TI Design, Synthesis, and Antiviral Activity of 2'-Deoxy-2'-fluoro-2'-C-methyl-cytidine, a Potent Inhibitor of Hepatitis C Virus Replication

AU Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stuyver, Lieven J.; Tharnish, Phillip M.; Lostia, Stefania; McBrayer, Tamara R.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Otto, Michael J.; Furman, Phillip A.; Stec, Wojciech J.; Patterson, Steven E.; Pankiewicz, Krzysztof W.

CS Pharmasset, Inc., Princeton, NJ, 08540, USA

SO Journal of Medicinal Chemistry (2005), 48(17), 5504-5508

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB The pyrimidine nucleoside-  $\beta$ -D-2'-deoxy-2'-fluoro-2'-C-methylcytidine (I) was designed as a hepatitis C virus RNA-dependent RNA polymerase (HCV RdRp) inhibitor. The title compound was obtained by a DAST fluorination of N4-benzoyl-1-(2-methyl-3,5-di-O-benzoyl- $\beta$ -D-arabinofuranosyl)cytosine to provide N4-benzoyl-1-(2-fluoro-2-methyl-3,5-di-O-benzoyl- $\beta$ -D-ribofuranosyl)cytosine. The protected 2'-C-methylcytidine was obtained as a byproduct from the DAST fluorination

and allowed for the preparation of two biol. active compds. from a common precursor. Compound I and 2'-C-methylcytidine were assayed in a sub-genomic HCV replicon assay system and found to be potent and selective inhibitors of HCV replication. Compd. I shows increased inhibitory activity in the HCV replicon assay compared to 2'-C-methylcytidine and low cellular toxicity.

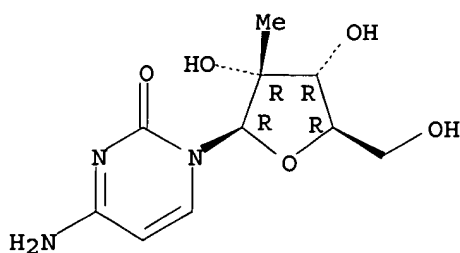
IT 20724-73-6

RL: PAC (Pharmacological activity); BIOL (Biological study)  
(design, synthesis via fluorination, and antiviral activity of  
2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of  
Hepatitis C virus replication)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



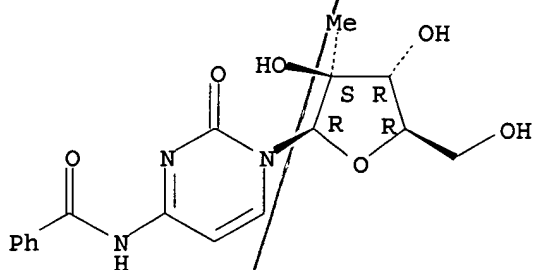
IT 817204-35-6P 863329-62-8P 863329-64-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(design, synthesis via fluorination, and antiviral activity of  
2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of  
Hepatitis C virus replication)

RN 817204-35-6 CAPLUS

CN Benzamide, N-[1,2-dihydro-1-(2-C-methyl-β-D-arabinofuranosyl)-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



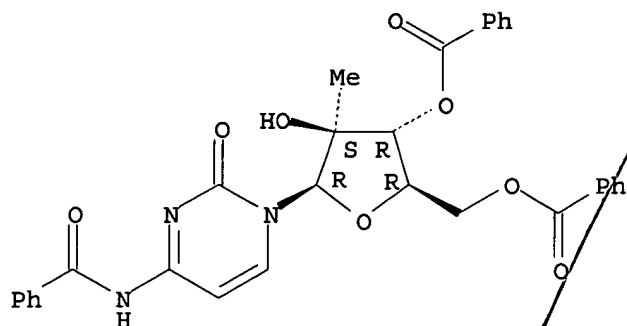
RN 863329-62-8 CAPLUS

CN Benzamide, N-[1-(3,5-di-O-benzoyl-2-C-methyl-β-D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



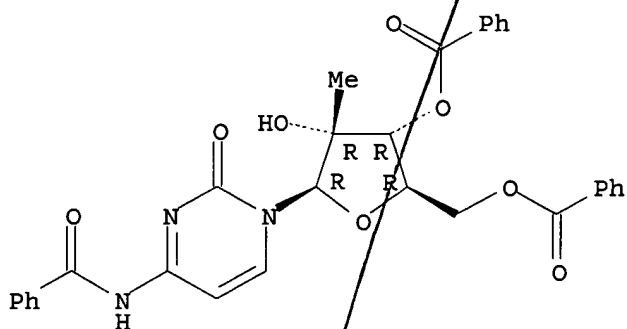
10/609,298



RN 863329-64-0 CAPLUS

CN Cytidine, N-benzoyl-2'-C-methyl-, 3',5'-dibenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2006 ACS on STM

AN 2005:34765 CAPLUS

DN 142:94074

TI Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogs as antiviral agents

IN Clark, Jeremy

PA Pharmasset, Ltd., Barbados

SO PCT Int. Appl., 228 pp.

CODEN: PIXXD2

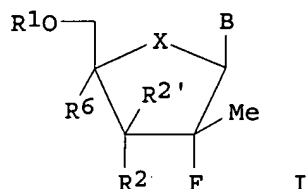
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005003147	A2	20050113	WO 2004-US12472	20040421
	WO 2005003147	A3	20050303		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,				

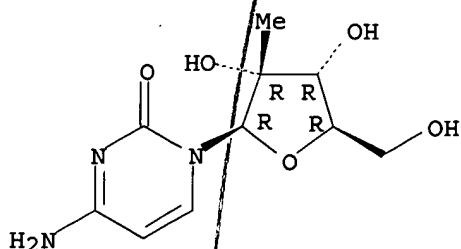
TD, TG  
 AU 2004253860 A1 20050113 AU 2004-253860 20040421  
 CA 2527657 AA 20050113 CA 2004-2527657 20040421  
 US 2005009737 A1 20050113 US 2004-828753 20040421  
 EP 1633766 A2 20060315 EP 2004-775900 20040421  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR  
 PRAI US 2003-474368P P 20030530  
 WO 2004-US12472 W 20040421  
 OS MARPAT 142:94074  
 GI



AB The disclosed invention provides nucleoside analogs I, wherein B is purine and pyrimidine nucleobase; X is O, S, CH<sub>2</sub>, Se, NH, N-alkyl, CHW, C(W)<sub>2</sub>; W is F, Cl, Br, iodo; R<sub>1</sub> is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar residue; R<sub>2</sub> and R<sub>2</sub>' are independently H, alkyl, alkenyl, alkynyl, vinyl, N<sub>3</sub>, CN, halogen, NO<sub>2</sub>, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R<sub>6</sub> is alkyl, CN, Me, OMe, OEt, CH<sub>2</sub>OH, CH<sub>2</sub>F, N<sub>3</sub>, CHCN, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NHMe, CH<sub>2</sub>NMe<sub>2</sub>, alkylne; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone marrow cells are reported. (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported.

IT 20724-73-6 374750-28-4  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)  
 RN 20724-73-6 CAPLUS  
 CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

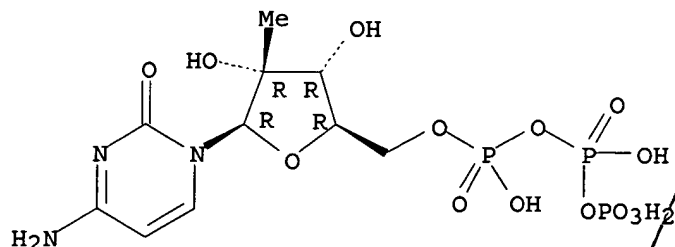


10/609,298

RN 374750-28-4 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 817204-35-6P 817204-36-7P

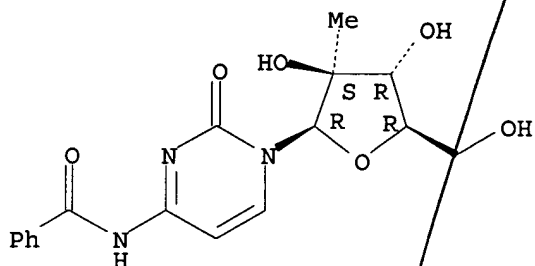
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

RN 817204-35-6 CAPLUS

CN Benzamide, N-[1,2-dihydro-1-(2-C-methyl-β-D-arabinofuranosyl)-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

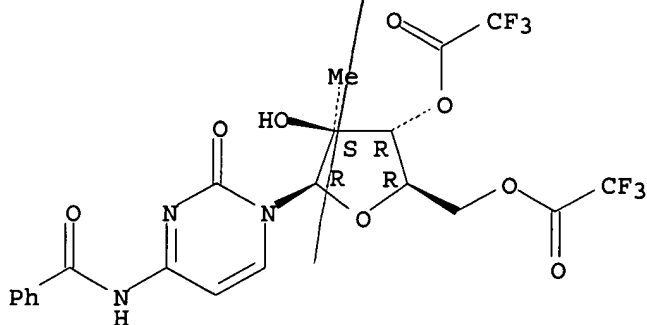
Absolute stereochemistry. Rotation (+).



RN 817204-36-7 CAPLUS

CN Benzamide, N-[1,2-dihydro-1-[2-C-methyl-3,5-bis-O-(trifluoroacetyl)-β-D-arabinofuranosyl]-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

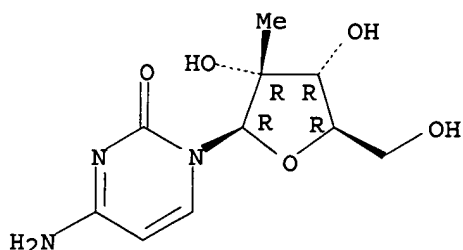


10/609,298

AN 2004:817630 CAPLUS  
DN 141:307495  
TI Use of nucleoside compounds and PALA for the treatment of  
flaviviridae infections  
IN Stuyver, Lieven J.  
PA Pharmasset Ltd., Barbados  
SO PCT Int. Appl., 120 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN. CNT 1

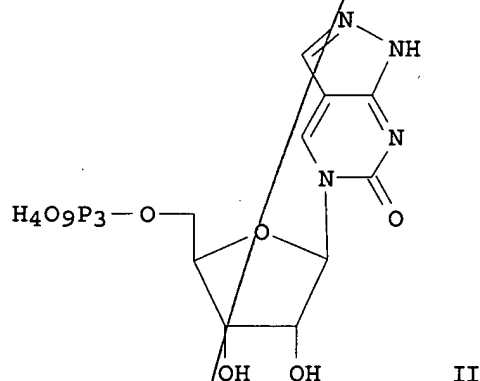
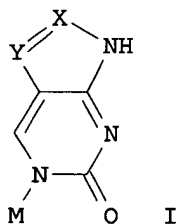
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004084796	A2	20041007	WO 2004-IB1429	20040329
	WO 2004084796	A3	20060406		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2004224575	A1	20041007	AU 2004-224575	20040329
	CA 2529311	AA	20041007	CA 2004-2529311	20040329
	US 2005049204	A1	20050303	US 2004-812448	20040329
	EP 1626692	A2	20060222	EP 2004-724085	20040329
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
PRAI	US 2003-458635P	P	20030328		
	WO 2004-IB1429	W	20040329		
OS	MARPAT 141:307495				
AB	The invention discloses a composition for and a method of treating Flaviviridae infections, e.g. bovine viral diarrhea virus, dengue Virus, West Nile virus, and hepatitis C virus, as well as abnormal cellular proliferation, in a host, including animals, and especially humans, using a nucleoside compound (Markush included) or N-(phosphonoacetyl)-L-aspartate (PALA), or a pharmaceutically acceptable salt or prodrug thereof.				
IT	20724-73-6				
	RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleoside compds. and PALA for treatment of flaviviridae infections)				
RN	20724-73-6 CAPLUS				
CN	Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)				

Absolute stereochemistry.



L8 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:780543 CAPLUS  
 DN 141:296247  
 TI Preparation of cytidine nucleoside analogs as antiviral agents  
 IN Girardet, Jean-Luc; Koh, Yung-Hyo; An, Haoyun; Hong, Zhi  
 PA Ribapharm Inc., USA  
 SO PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004080466	A1	20040923	WO 2003-US6992	20030307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003225705	A1	20040930	AU 2003-225705	20030307
PRAI WO 2003-US6992	A	20030307		
OS MARPAT 141:296247				
GI				



AB Cytidine analogs I, wherein -X=Y- is -N=N-, -CH=N-, -N=CZ- or -CH=CZ-, wherein Z is H, halogen, or alkyl, and wherein M is a sugar or sugar analog; wherein the compound has a D-configuration or an L-configuration; with the proviso that where M is a substituted sugar with a ribofuranose ring having a heteroatom and substituents R1 and R2 on the C3'-atom, R3 and R4 on the C2'-atom, and R5 on the C5'-atom, R1-R4 together are not independently H, OH, F, NH<sub>2</sub>, N<sub>3</sub>, O-hydrocarbyl, or a reporter moiety, when the heteroatom is O, S, Se, SO, N-alkyl, or CH<sub>2</sub>, and when R5 is OH, SH, NH<sub>2</sub>, monophosphate, diphosphate, triphosphate, thiophosphate, or boranophosphate; and with the further proviso that M does not comprise a cyclopropenyl group, a morpholino group, or M is not a phosphorylmethoxyethyl, their prodrugs and/or metabolites are employed as pharmaceutically active compds. for treatment of diseases responsive to such compds. Particularly preferred diseases include viral diseases

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(e.g., HCV infection) and neoplasms (no biol. data). Thus nucleoside analog II was prepared and tested as antiviral agent. The virus is an HCV virus, an HIV virus, an RSV virus, an influenza virus, or a an HBV virus.

IT 760965-44-4P

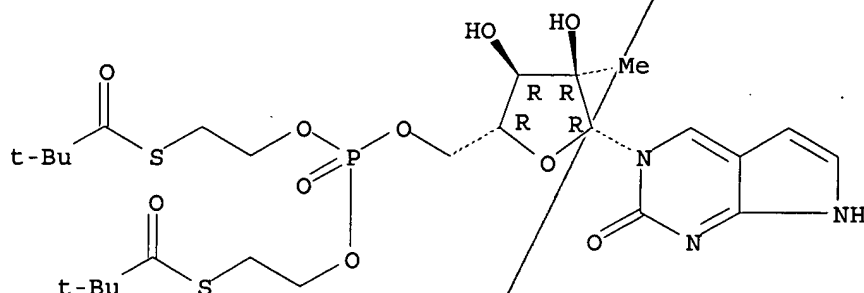
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of cytidine nucleoside analogs as antiviral agents)

RN 760965-44-4 CAPLUS

CN 2H-Pyrrolo[2,3-d]pyrimidin-2-one, 3-[5-O-[bis[2-[(2,2-dimethyl-1-oxopropyl)thio]ethoxy]phosphinyl]-2-C-methyl-β-D-ribofuranosyl]-1,3-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 760965-41-1P 760965-42-2P 760965-52-4P

760965-53-5P 760965-54-6P 760965-55-7P

760965-56-8P 760965-62-6P

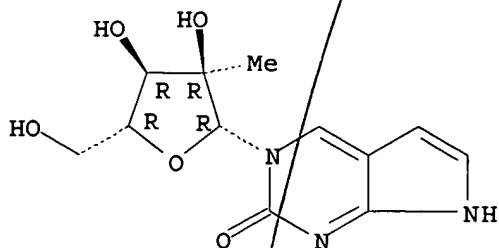
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of cytidine nucleoside analogs as antiviral agents)

RN 760965-41-1 CAPLUS

CN 2H-Pyrrolo[2,3-d]pyrimidin-2-one, 1,3-dihydro-3-(2-C-methyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

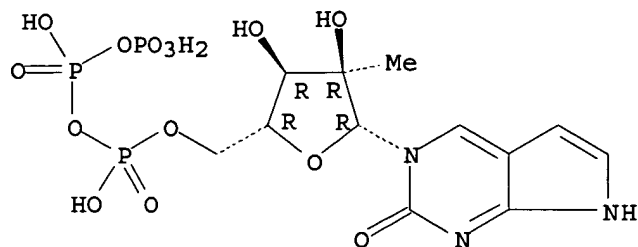


RN 760965-42-2 CAPLUS

CN 2H-Pyrrolo[2,3-d]pyrimidin-2-one, 1,3-dihydro-3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-2-C-methyl-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

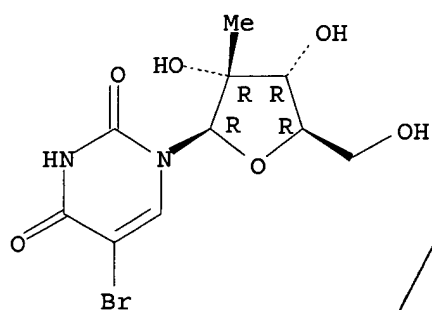
10/609,298



RN 760965-52-4 CAPLUS

CN Uridine, 5-bromo-2'-C-methyl- (9CI) (CA INDEX NAME)

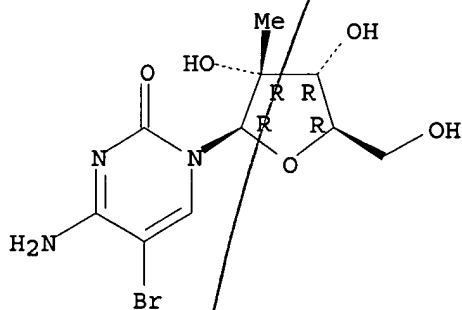
Absolute stereochemistry.



RN 760965-53-5 CAPLUS

CN Cytidine, 5-bromo-2'-C-methyl- (9CI) (CA INDEX NAME)

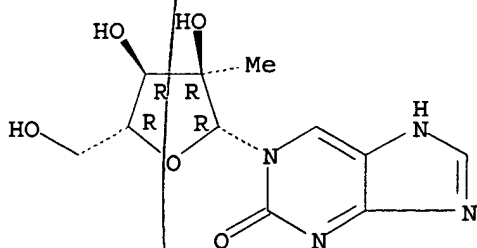
Absolute stereochemistry.



RN 760965-54-6 CAPLUS

CN 2H-Purin-2-one, 1,3-dihydro-1-(2-C-methyl-β-D-ribofuranosyl)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

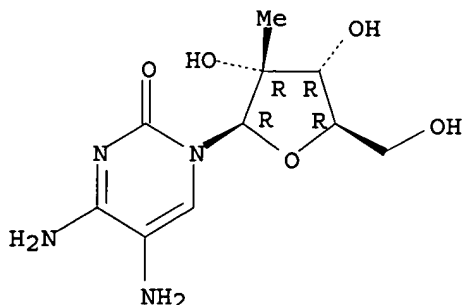


10/609,298

RN 760965-55-7 CAPLUS

CN Cytidine, 5-amino-2'-C-methyl- (9CI) (CA INDEX NAME)

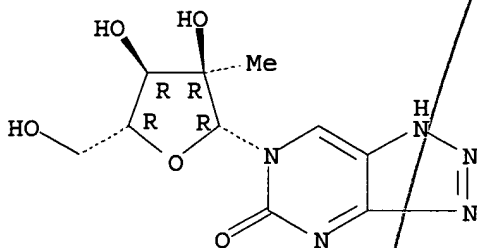
Absolute stereochemistry.



RN 760965-56-8 CAPLUS

CN 5H-1,2,3-Triazolo[4,5-d]pyrimidin-5-one, 1,6-dihydro-6-(2-C-methyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

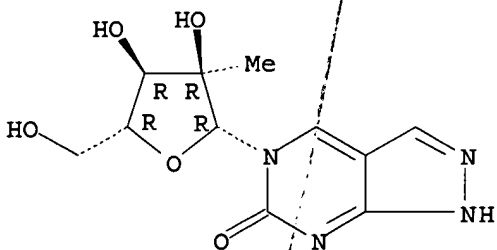
Absolute stereochemistry.



RN 760965-62-6 CAPLUS

CN 6H-Pyrazolo[3,4-d]pyrimidin-6-one, 1,5-dihydro-5-(2-C-methyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:652668 CAPLUS

DN 141:167739

TI Diribonucleotides as specific viral RNA-polymerase inhibitors for the treatment or prevention of viral infections

IN Wu, Jim Zhen; An, Haoyun; Hong, Zhi

PA USA



10/609,298

SO U.S. Pat. Appl. Publ., 12 pp.

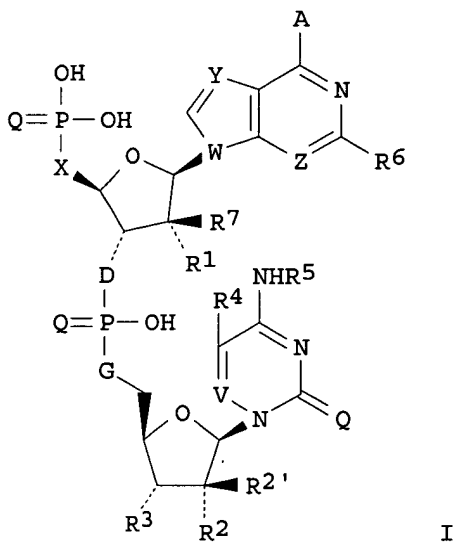
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004158054	A1	20040812	US 2003-360218	20030207
PRAI	US 2003-360218		20030207		
OS	MARPAT 141:167739				
GI					



AB The invention discloses compds. and methods using dinucleotide compds. I (A = H, OR, SR, NH<sub>2</sub>, or NHR; Q = O or S; V, W, Y, and Z = CH or N; X = O, S, NR, etc.; D and G = null, CH<sub>2</sub>, O, etc.; R<sub>1</sub>, R<sub>2</sub>, R<sub>2</sub>', R<sub>3</sub> = H, OR, halogen, CF<sub>3</sub> etc.; R<sub>4</sub> = R; R<sub>5</sub> = H, NH<sub>2</sub>, NHR, etc.; R<sub>6</sub> = H, NH<sub>2</sub>, NHCOR, etc.; R<sub>7</sub> = H, OR, SR, halogen, etc.; R = H, (un)substituted alkyl, aryl, etc.) comprising a first and second nucleoside. The dinucleotide inhibits viral RNA polymerase and at least one of the nucleosides exhibits antiviral activity when cleaved from the dinucleotide.

IT 735268-87-8P

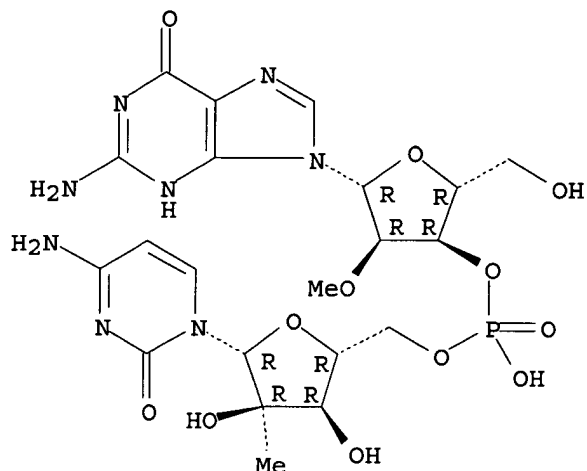
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(diribonucleotides as specific viral RNA-polymerase inhibitors for treatment or prevention of viral infections)

RN 735268-87-8 CAPLUS

CN Cytidine, 2'-O-methylguanylyl-(3'→5')-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 735268-88-9

RL: RCT (Reactant); RACT (Reactant or reagent)

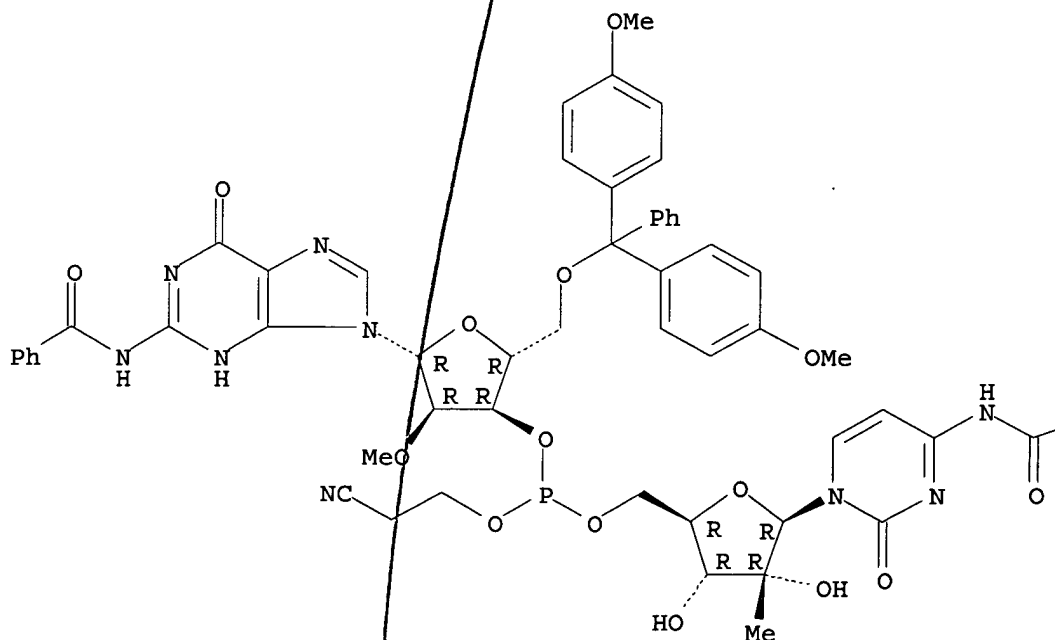
(diribonucleotides as specific viral RNA-polymerase inhibitors for treatment or prevention of viral infections)

RN 735268-88-9 CAPLUS

CN Cytidine, N-benzoyl-5'-O- [bis (4-methoxyphenyl) phenylmethyl] -P(O) - (2-cyanoethyl) -P-doxo-2'-O-methylguanylyl- (3'→5') -N-benzoyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

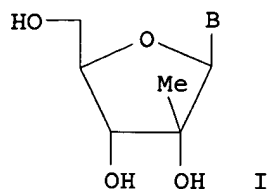
PAGE 1-A



Ph

L8 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:566635 CAPLUS  
 DN 141:89323  
 TI Process for the production of 3'-nucleoside prodrugs  
 IN Storer, Richard; Moussa, Adel; Mathieu, Steven; Qu, Lin  
 PA Idenix Cayman Limited, Cayman I.  
 SO PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058792	A1	20040715	WO 2003-US41603	20031223
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2511616	AA	20040715	CA 2003-2511616	20031223
	AU 2003300434	A1	20040722	AU 2003-300434	20031223
	US 2004181051	A1	20040916	US 2003-746395	20031223
	EP 1575971	A1	20050921	EP 2003-814400	20031223
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016868	A	20051025	BR 2003-16868	20031223
	CN 1751058	A	20060322	CN 2003-80109820	20031223
	JP 2006514038	T2	20060427	JP 2004-562599	20031223
	NO 2005003557	A	20050908	NO 2005-3557	20050720
PRAI	US 2002-436150P	P	20021223		
	WO 2003-US41603	W	20031223		
OS	CASREACT 141:89323		MARPAT 141:89323		
GI					



AB Provided is a single-step process for the regioselective 3'-acylation of a ribofuranosyl 2'- or 3'-branched nucleosides I, wherein B is nucleobase. These compds. are useful as antiviral agents, and in particular, can be used to treat Flaviviridae infections in a host in need thereof (no data). Thus, 9-(2'-C-methyl-3'-O-valinoyl- $\beta$ -D-ribofuranosyl)-6-N-methyladenine dihydrochloride was prepared via regioselective esterification of 9-(2'-C-methyl- $\beta$ -D-ribofuranosyl)-6-N-methyladenine with N-(tert-butoxycarbonyl)-L-valine.

IT 640725-70-8P

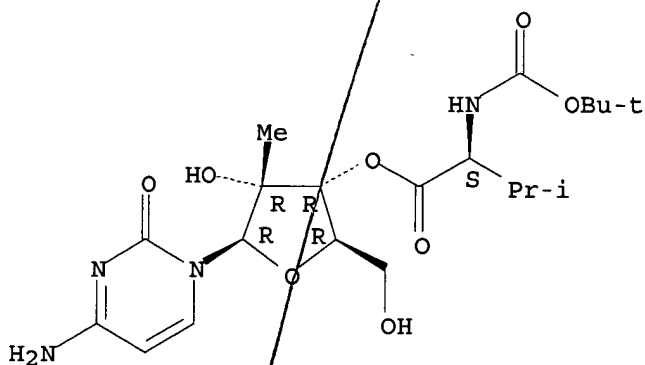
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for production of nucleoside prodrugs via regioselective esterification)

RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 20724-73-6

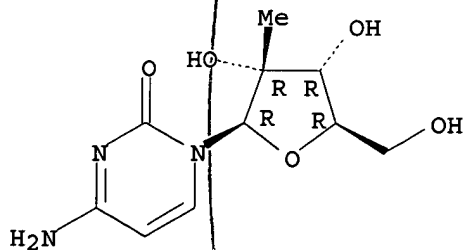
RL: RCT (Reactant); RACT (Reactant or reagent)

(process for production of nucleoside prodrugs via regioselective esterification)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:453348 CAPLUS  
 DN 141:17578  
 TI Treatment of Flaviviridae infection with 2'-branched nucleosides  
 and another mutation-inducing drug such as interferon  
 IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standring, David; Bichko, Vadim;  
 Qu, Lin  
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari  
 SO PCT Int. Appl., 166 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046331	A2	20040603	WO 2003-US36714	20031117
	WO 2004046331	A3	20060302		
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	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,				
	GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,				
	LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,				
	OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,				
	TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				
	BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				
	ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,				
	TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2506129	AA	20040603	CA 2003-2506129	20031117
	AU 2003298658	A1	20040615	AU 2003-298658	20031117
	US 2005031588	A1	20050210	US 2003-715729	20031117
	EP 1576138	A2	20050921	EP 2003-796412	20031117
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016363	A	20051004	BR 2003-16363	20031117
	NO 2005002920	A	20050815	NO 2005-2920	20050615
PRAI	US 2002-426675P	P	20021115		
	WO 2003-US36714	W	20031117		

OS MARPAT 141:17578

AB The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT, of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with  $\beta$ -D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon  $\alpha$ -2b). Intron A and  $\beta$ -D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.

IT 20724-73-6

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

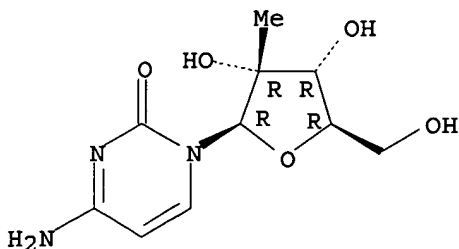
(treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 20724-73-6 CAPLUS

10/609,298

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



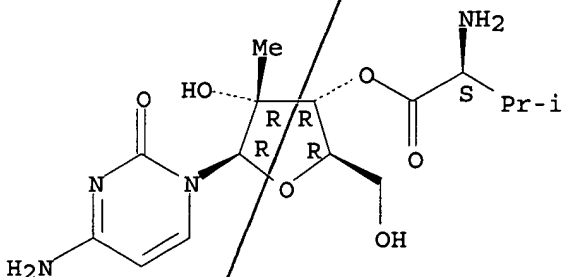
IT 640281-90-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(treatment of Flaviviridae infection with 2'-branched  
nucleosides and another mutation-inducing drug such as interferon)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:20697 CAPLUS

DN 140:87662

TI 2'- and 3'-nucleoside prodrugs for treating Flaviviridae  
infections

IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin,  
Gilles

PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche  
Scientifique; Universita Degli Studi di Cagliari

SO PCT Int. Appl., 2498 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN. CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004003000	A2	20040108	WO 2003-IB3901	20030627
	WO 2004003000	A3	20041104		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2490200 AA 20040108 CA 2003-2490200 20030627  
AU 2003263412 A1 20040119 AU 2003-263412 20030627  
EP 1525209 A2 20050427 EP 2003-761749 20030627  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1678621 A 20051005 CN 2003-820690 20030627  
JP 2005537242 T2 20051208 JP 2004-517162 20030627  
CN 1761677 A 20060419 CN 2003-820501 20030627  
WO 2005020884 A2 20050310 WO 2004-US15395 20040514  
WO 2005020884 A3 20060622

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1656093 A2 20060517 EP 2004-776022 20040514  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

NO 2005000466 A 20050323 NO 2005-466 20050127

PRAI US 2002-392350P P 20020628  
US 2002-392351P P 20020628  
US 2003-466194P P 20030428  
US 2003-470949P P 20030514  
WO 2003-IB3901 W 20030627  
WO 2004-US15395 W 20040514

OS MARPAT 140:87662

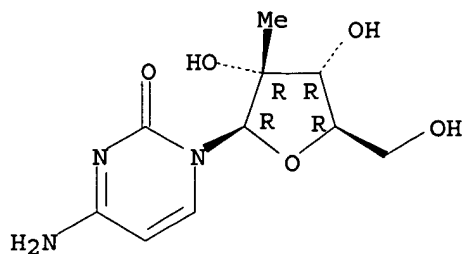
AB 2' And 3'-Prodrugs of 1'-, 2'-, 3'-, or 4'-branched  $\beta$ -D or  $\beta$ -L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Comps., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included.

IT 20724-73-6P  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 20724-73-6 CAPLUS  
CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/609,298



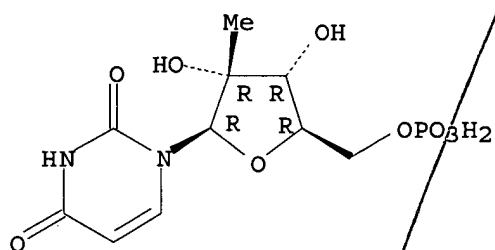
IT 125911-78-6 386213-38-3

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 125911-78-6 CAPLUS

CN 5'-Uridylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

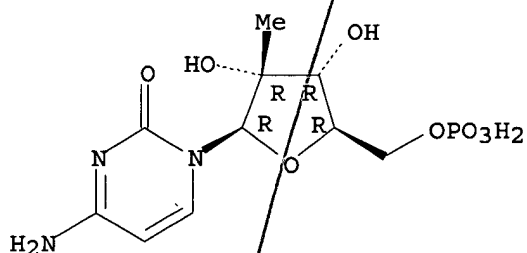
Absolute stereochemistry.



RN 386213-38-3 CAPLUS

CN 5'-Cytidylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 125911-76-4 150993-73-0 640725-72-0

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
BIOL (Biological study)  
(nucleoside prodrugs for treating Flaviviridae infections)

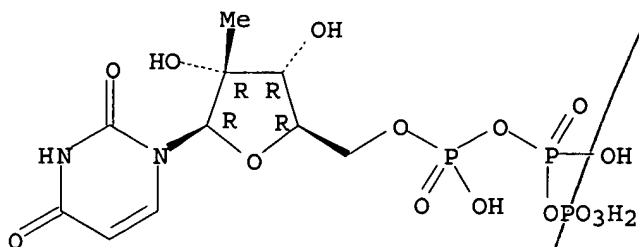
RN 125911-76-4 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



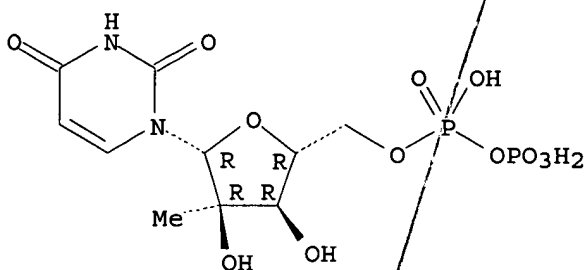
10/609,298



RN 150993-73-0 CAPLUS

CN Uridine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

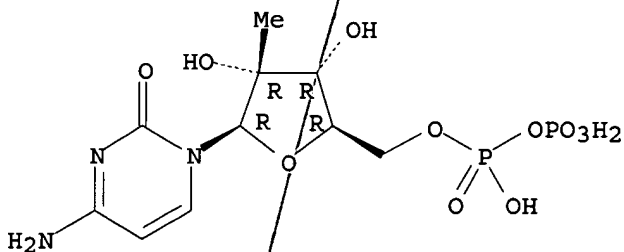
Absolute stereochemistry.



RN 640725-72-0 CAPLUS

CN Cytidine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 374750-28-4

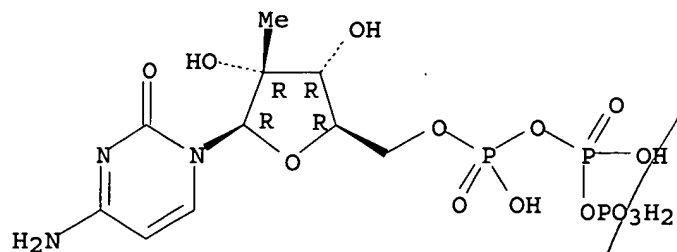
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
PKT (Pharmacokinetics); BIOL (Biological study)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 374750-28-4 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/609,298



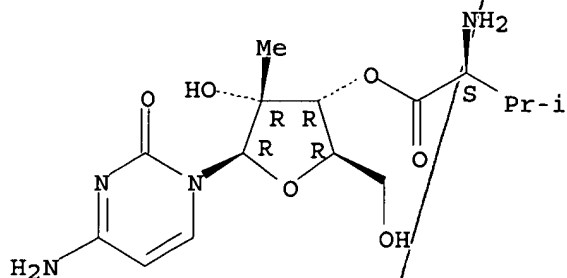
IT 640725-71-9P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

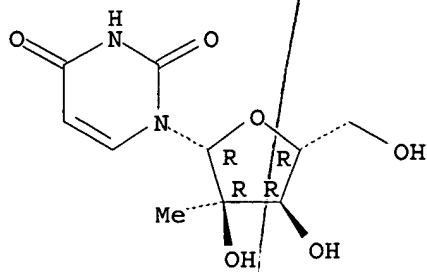
IT 31448-54-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections)

RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-70-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

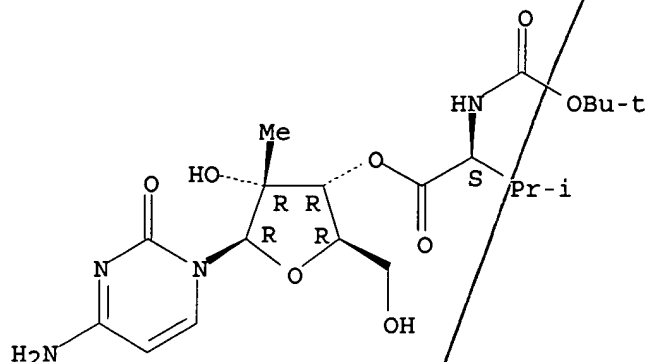
10/609,298

(nucleoside prodrugs for treating Flaviviridae infections)

RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



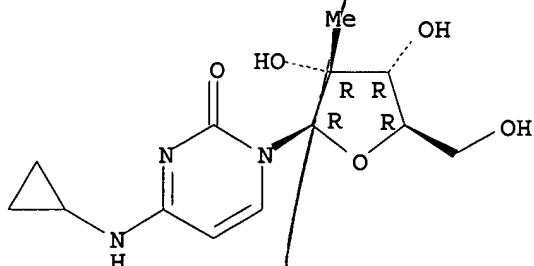
IT 622381-09-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nucleoside prodrugs for treating Flaviviridae infections,  
and use with other agents)

RN 622381-09-3 CAPLUS

CN Cytidine, N-cyclopropyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:20696 CAPLUS

DN 140:77365

TI Preparation of modified 2'- and 3'-nucleoside prodrugs for treating  
Flaviviridae infections

IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin,  
Gilles

PA Idenix (Cayman) Limited, Cayman I.; Universita degli studi di Cagliari;  
Centre National de la Recherche Scientifique

SO PCT Int. Appl., 201 pp.

CODEN: PIXXD2

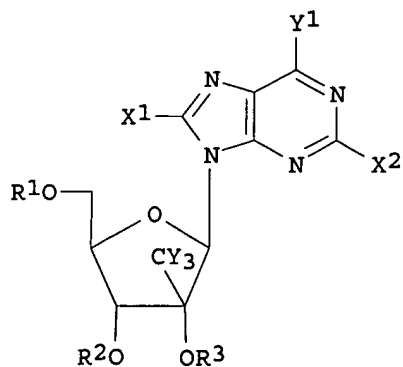
DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004002999	A2	20040108	WO 2003-IB3246	20030627

WO 2004002999	A3	20040812	
WO 2004002999	C1	20050217	
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
CA 2490191	AA	20040108	CA 2003-2490191 20030627
AU 2003247084	A1	20040119	AU 2003-247084 20030627
EP 1523489	A2	20050420	EP 2003-761744 20030627
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CN 1678621	A	20051005	CN 2003-820690 20030627
JP 2005533817	T2	20051110	JP 2004-517158 20030627
CN 1761677	A	20060419	CN 2003-820501 20030627
WO 2005020884	A2	20050310	WO 2004-US15395 20040514
WO 2005020884	A3	20060622	
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EP 1656093	A2	20060517	EP 2004-776022 20040514
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR		
NO 2005000465	A	20050127	NO 2005-465 20050127
PRAI US 2002-392350P	P	20020628	
US 2002-392351P	P	20020628	
US 2003-466194P	P	20030428	
US 2003-470949P	P	20030514	
WO 2003-IB3246	W	20030627	
WO 2004-US15395	W	20040514	
OS			
GI			



AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, OR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Comps. and compns. of the prodrugs of the present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of  $\beta$ -D-2'-C-methyl-7-methyl-6-phenyl-3,3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

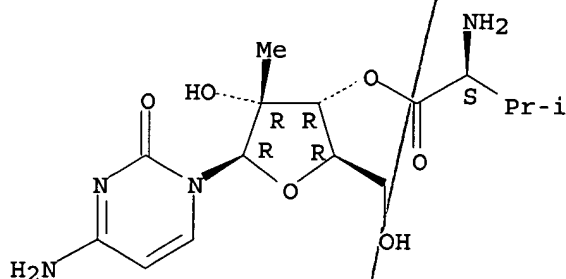
IT 640281-90-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of modified and nucleoside prodrugs for treating flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



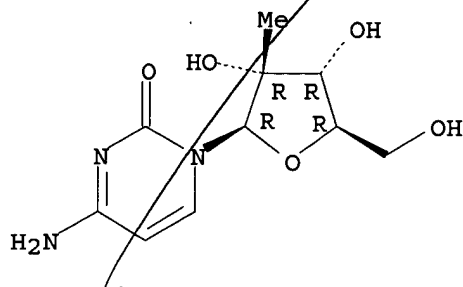
IT 20724-73-6

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of modified and nucleoside prodrugs for treating flaviviridae infections)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:20443 CAPLUS  
 DN 140:70984  
 TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of  
 flaviviridae infections  
 IN Sommadossi, Jean-Pierre; La Colla, Paolo  
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari  
 SO PCT Int. Appl., 110 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English

FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004002422	A2	20040108	WO 2003-US20431	20030627
WO 2004002422	A3	20050407		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2489552	AA	20040108	CA 2003-2489552	20030627
AU 2003248748	A1	20040119	AU 2003-248748	20030627
US 2004077587	A1	20040422	US 2003-607909	20030627
EP 1536804	A2	20050608	EP 2003-762183	20030627
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1678326	A	20051005	CN 2003-820701	20030627
JP 2005533824	T2	20051110	JP 2004-518041	20030627
WO 2005020884	A2	20050310	WO 2004-US15395	20040514
WO 2005020884	A3	20060622		
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1656093	A2	20060517	EP 2004-776022	20040514
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			

10/609,298

NO 2005000490	A	20050127	NO 2005-490	20050127
PRAI US 2002-392351P	P	20020628		
US 2003-466194P	P	20030428		
US 2003-470949P	P	20030514		
WO 2003-US20431	W	20030627		
WO 2004-US15395	W	20040514		

OS MARPAT 140:70984

AB The 3'-L-valine ester of  $\beta$ -D-2'-C-methyl-ribofuranosyl cytidine provides superior results against flaviviruses and pestiviruses, including hepatitis C virus. Based on this discovery, compds., compns., methods and uses are provided for the treatment of flaviviridae, including HCV, that include the administration of an effective amount of val-mCyd or its salt, ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound

IT 640281-90-9D, salts 642075-50-1 642075-51-2

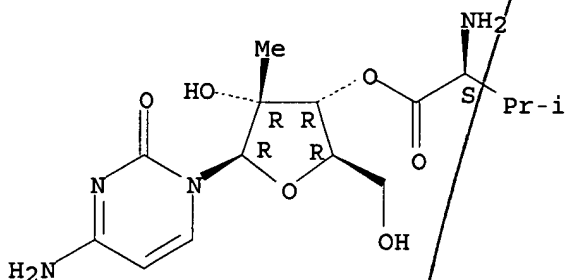
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642075-64-7 642075-65-8 642075-66-9  
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642075-70-5 642075-71-6 642075-72-7  
642075-74-9 642075-75-0 642075-76-1  
642075-77-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ribofuranosylcytidine methylvaline ester combined with other  
antivirals for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 642075-50-1 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 4-methylbenzenesulfonate (salt) (9CI) (CA INDEX NAME)

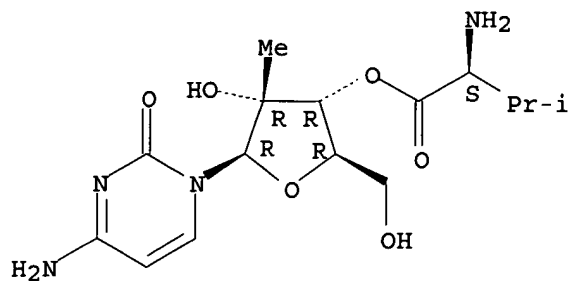
CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

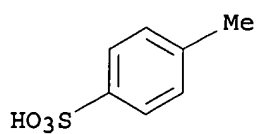
10/609,298



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



RN 642075-51-2 CAPLUS

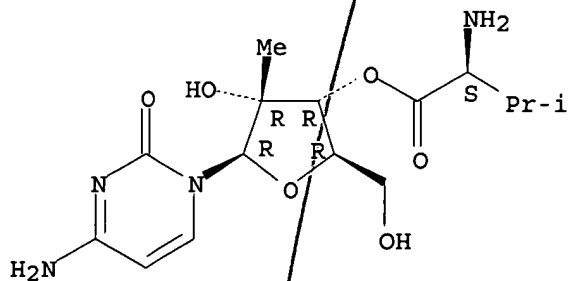
CN L-Valine, 3'-ester with 2'-C-methylcytidine, methanesulfonate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

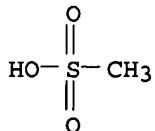
Absolute stereochemistry.



CM 2

CRN 75-75-2

CMF C H4 O3 S





10/609,298

RN 642075-52-3 CAPLUS

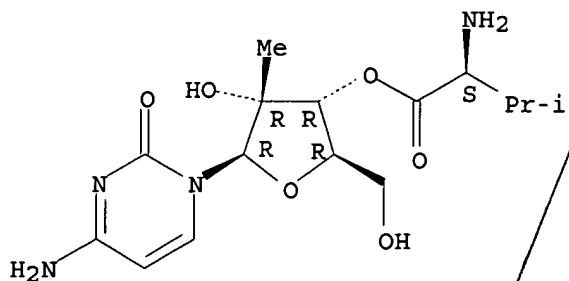
CN L-Valine, 3'-ester with 2'-C-methylcytidine, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

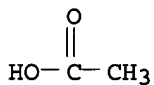
Absolute stereochemistry.



CM 2

CRN 64-19-7

CMF C2 H4 O2



RN 642075-53-4 CAPLUS

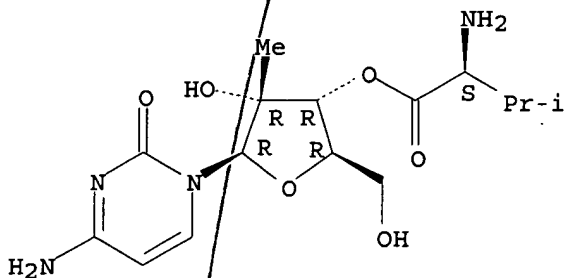
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

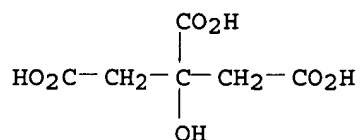


CM 2

CRN 77-92-9

10/609,298

CMF C6 H8 O7



RN 642075-54-5 CAPLUS

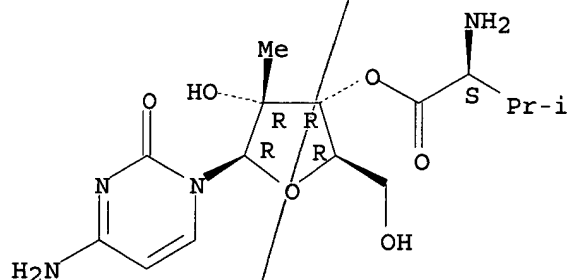
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanedioate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

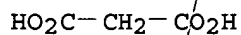
Absolute stereochemistry.



CM 2

CRN 141-82-2

CMF C3 H4 O4



RN 642075-55-6 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

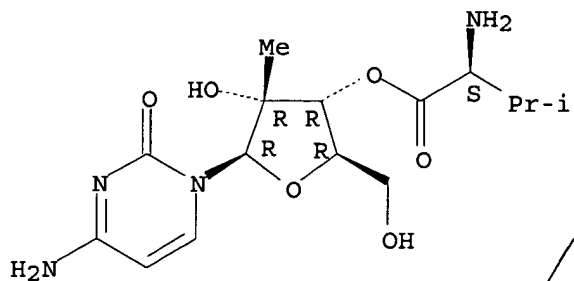
CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

10/609,298

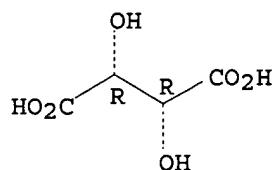


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



RN 642075-56-7 CAPLUS

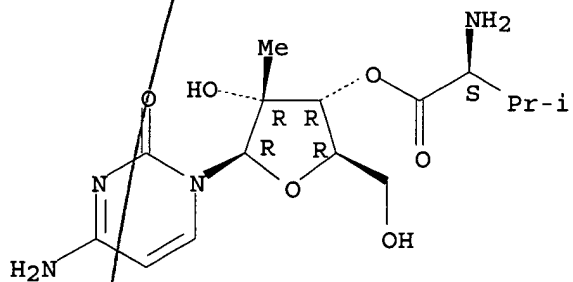
CN L-Valine, 3'-ester with 2'-C-methylcytidine, butanedioate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

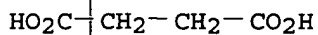
Absolute stereochemistry.



CM 2

CRN 110-15-6

CMF C4 H6 O4



RN 642075-57-8 CAPLUS

10/609,298

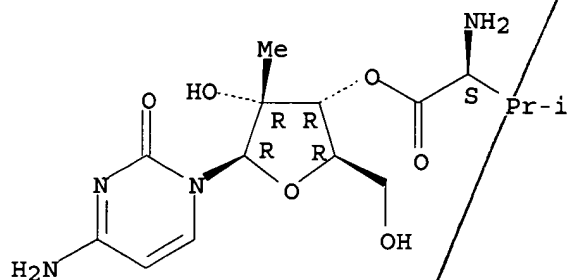
CN L-Valine, 3'-ester with 2'-C-methylcytidine, benzoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

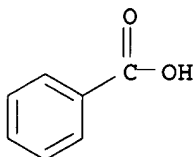
Absolute stereochemistry.



CM 2

CRN 65-85-0

CMF C7 H6 O2



RN 642075-58-9 CAPLUS

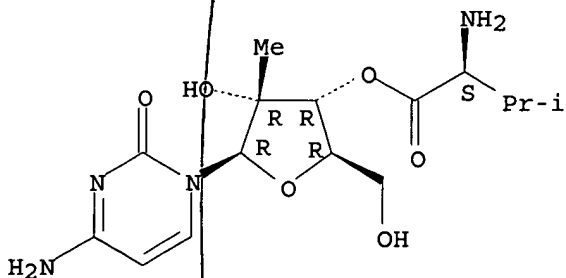
CN L-Ascorbic acid, compd. with L-valine 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

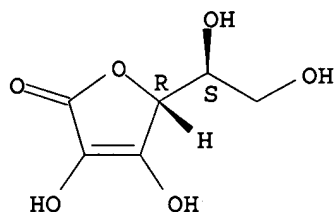


CM 2

10/609,298

CRN 50-81-7  
CMF C6 H8 O6

Absolute stereochemistry.

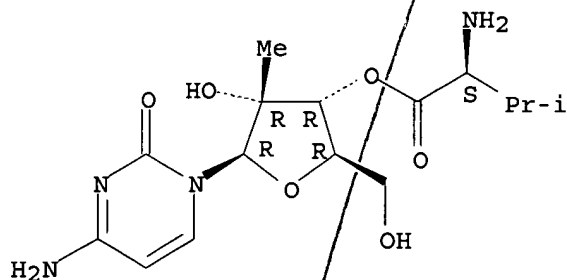


RN 642075-59-0 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopentanedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

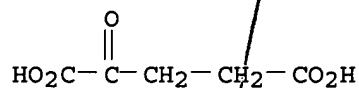
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 328-50-7  
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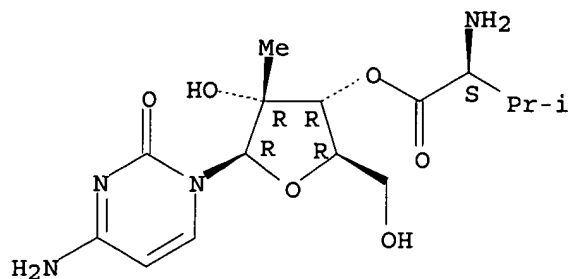
RN 642075-60-3 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2,3-dihydroxypropyl phosphate  
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry.

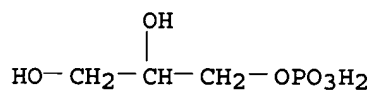
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CM 2

CRN 57-03-4

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RN 642075-61-4 CAPLUS

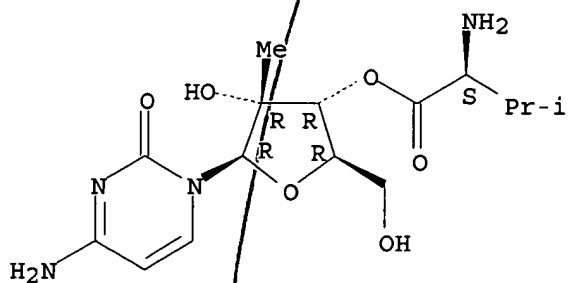
CN L-Valine, 3'-ester with 2'-C-methylcytidine, formate (salt) (9CI) (CA INDEX NAME)

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CRN 640281-90-9

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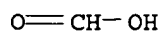
Absolute stereochemistry.



CM 2

CRN 64-18-6

CMF C H2 O2



RN 642075-62-5 CAPLUS

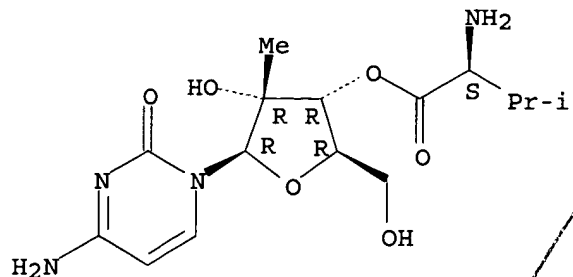
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2E)-2-butenedioate (salt) (9CI) (CA INDEX NAME)

CM 1

10/609,298

CRN 640281-90-9  
CMF C15 H24 N4 O6

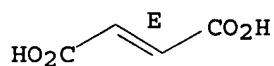
Absolute stereochemistry.



CM 2

CRN 110-17-8  
CMF C4 H4 O4

Double bond geometry as shown.

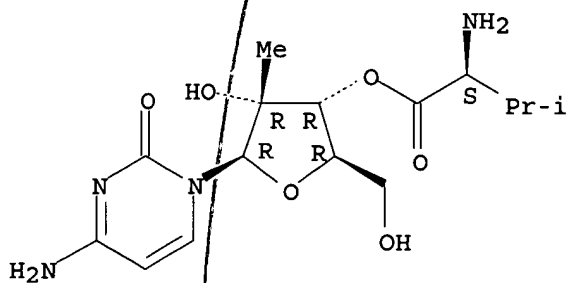


RN 642075-63-6 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanoate (salt) (9CI) (CA  
INDEX NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

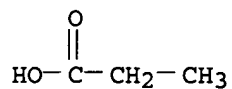
Absolute stereochemistry.



CM 2

CRN 79-09-4  
CMF C3 H6 O2

10/609,298

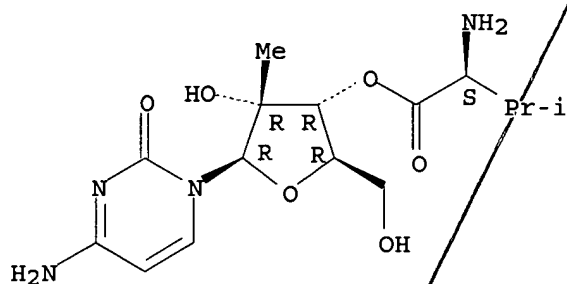


RN 642075-64-7 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydroxyacetate (salt) (9CI)  
(CA INDEX NAME)

CM 1

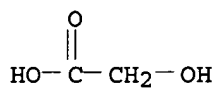
CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 79-14-1  
CMF C2 H4 O3

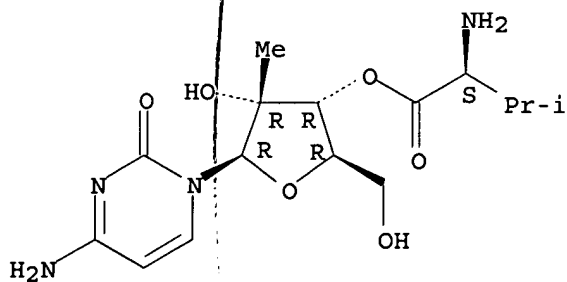


RN 642075-65-8 CAPLUS  
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxypropanoate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9  
CMF C15 H24 N4 O6

Absolute stereochemistry.



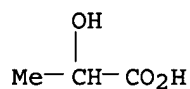


10/609,298

CM 2

CRN 50-21-5

CMF C3 H6 O3



RN 642075-66-9 CAPLUS

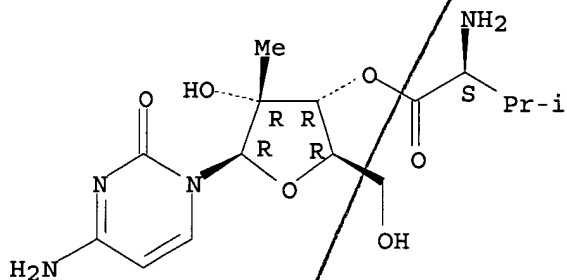
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopropanoate (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

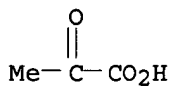
Absolute stereochemistry.



CM 2

CRN 127-17-3

CMF C3 H4 O3



RN 642075-67-0 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, ethanedioate (salt) (9CI)  
(CA INDEX NAME)

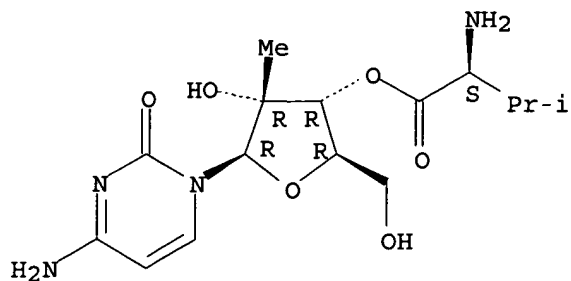
CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

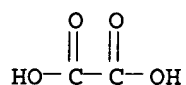
10/609,298



CM 2

CRN 144-62-7

CMF C2 H2 O4



RN 642075-68-1 CAPLUS

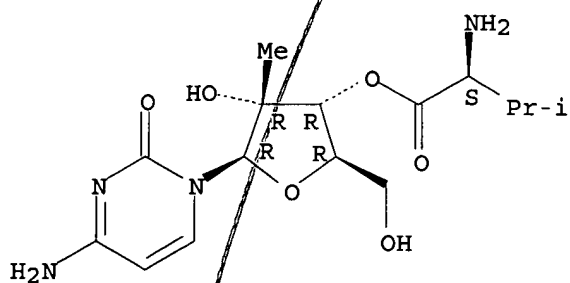
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2Z)-2-butenedioate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

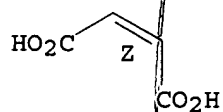


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RN 642075-69-2 CAPLUS

10/609,298

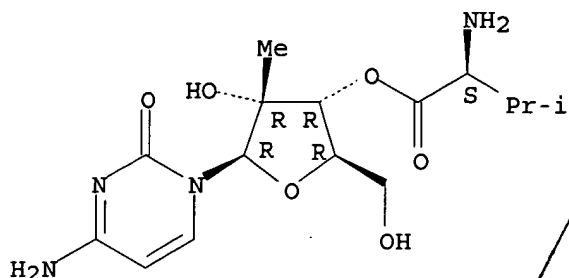
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxybenzoate (salt)  
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

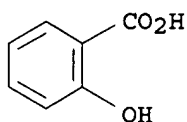
Absolute stereochemistry.



CM 2

CRN 69-72-7

CMF C7 H6 O3



RN 642075-70-5 CABLUS

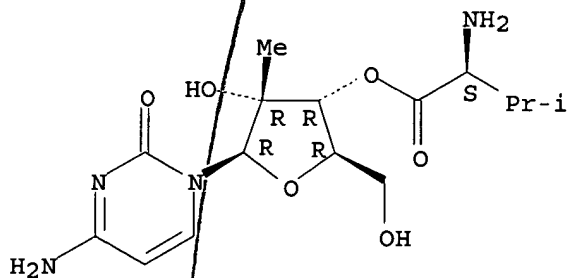
CN L-Valine, 3'-ester with 2'-C-methylcytidine, sulfate (salt) (9CI) (CA  
INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

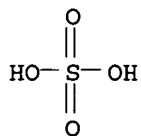


CM 2

CRN 7664-93-9

10/609,298

CMF H2 O4 S



RN 642075-71-6 CAPLUS

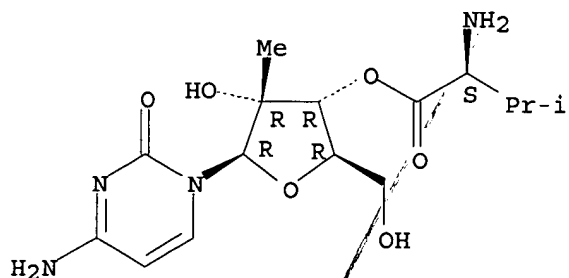
CN L-Valine, 3'-ester with 2'-C-methylcytidine, nitrate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

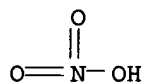
Absolute stereochemistry.



CM 2

CRN 7697-37-2

CMF H N O3



RN 642075-72-7 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (salt) (9CI) (CA INDEX NAME)

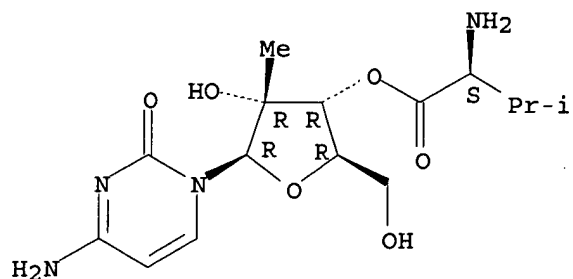
CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

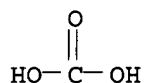
10/609,298



CM 2

CRN 463-79-6

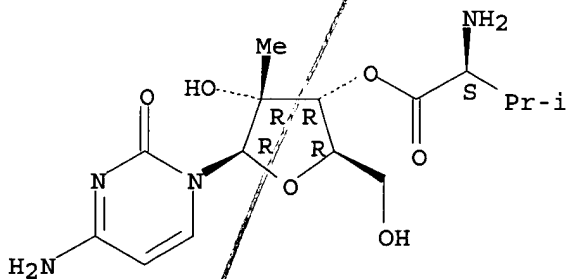
CMF C H2 O3



RN 642075-74-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



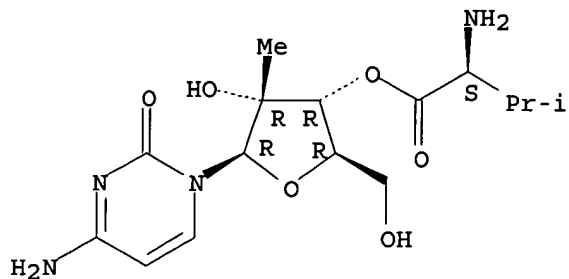
● x HBr

RN 642075-75-0 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydriodide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/609,298



●x HI

RN 642075-76-1 CAPLUS

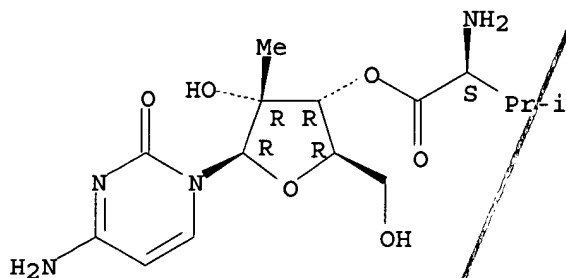
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (2:1) (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

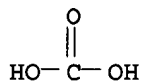
Absolute stereochemistry.



CM 2

CRN 463-79-6

CMF C H2 O3



RN 642075-77-2 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, phosphate (salt) (9CI) (CA  
INDEX NAME)

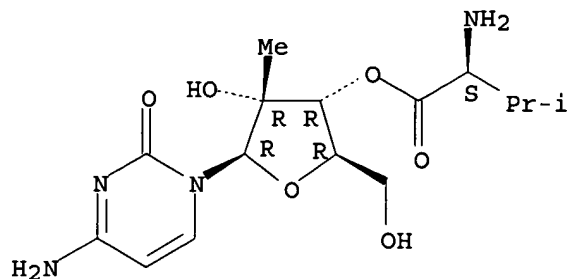
CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

Absolute stereochemistry.

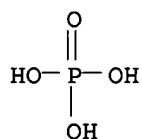
10/609,298



CM 2

CRN 7664-38-2

CMF H3 O4 P



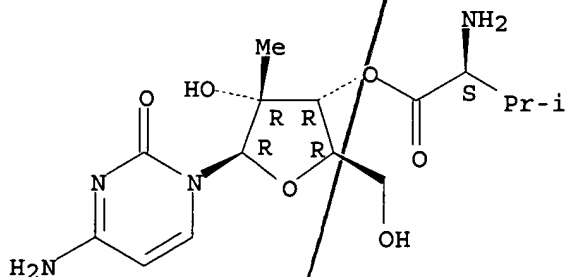
IT 640281-90-9P

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 20724-73-6P 640725-70-8P 642075-42-1P

642075-43-2P 642075-44-3P

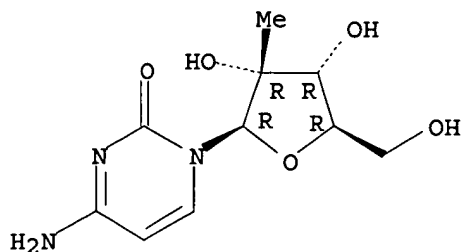
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

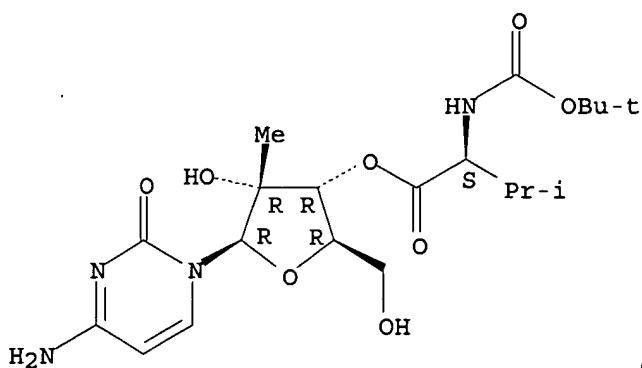
10/609,298



RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

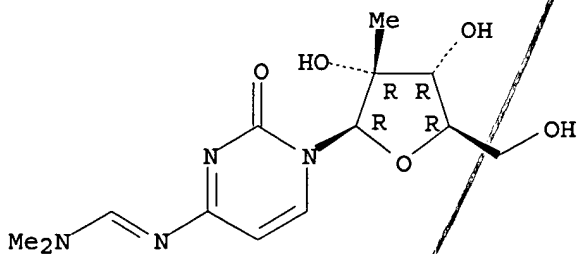


RN 642075-42-1 CAPLUS

CN Cytidine, N-[(dimethylamino)methylene]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



RN 642075-43-2 CAPLUS

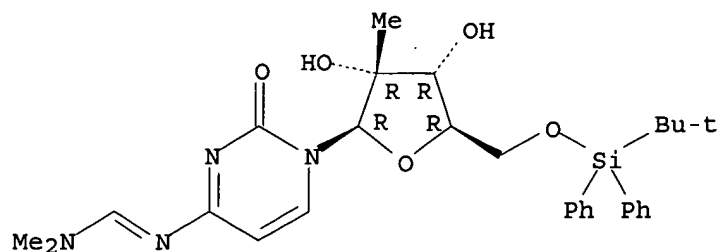
CN Cytidine, N-[(dimethylamino)methylene]-5'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



10/609,298

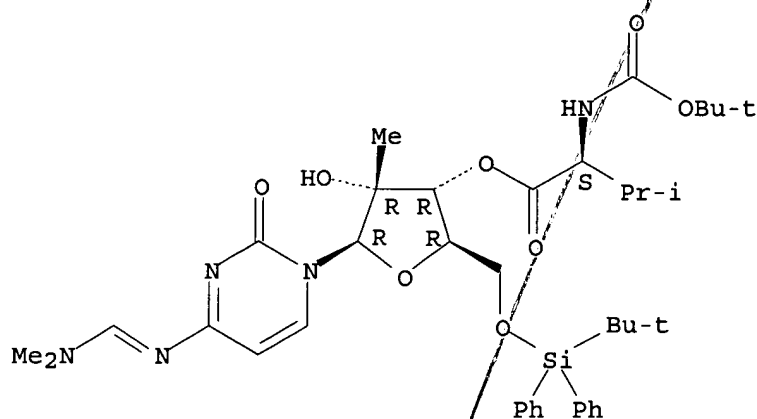


RN 642075-44-3 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with  
5'-O-[(1,1-dimethylethyl)diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-  
methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



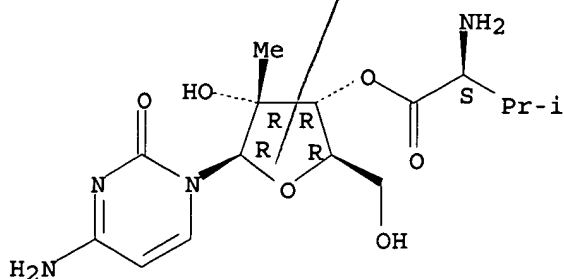
IT 640725-71-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(ribofuranosylcytidine methylvaline ester for treatment of  
flaviviridae infections)

RN 640725-71-9 CAPLUS

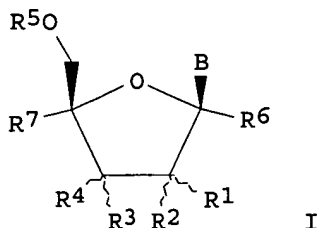
CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:2898 CAPLUS  
 DN 140:42424  
 TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA viral polymerase  
 IN Carroll, Steven S.; Olsen, David B.; Durette, Philippe L.; Bhat, Balkrishen; Dande, Prasad; Eldrup, Anne B.  
 PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.  
 SO PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000858	A2	20031231	WO 2003-US19172	20030617
	WO 2004000858	A3	20050512		
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	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2488534	AA	20031231	CA 2003-2488534	20030617
	AU 2003269890	A1	20040106	AU 2003-269890	20030617
	EP 1551421	A2	20050713	EP 2003-751777	20030617
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005530843	T2	20051013	JP 2004-515870	20030617
PRAI	US 2002-390579P	P	20020621		
	WO 2003-US19172	W	20030617		
OS	MARPAT 140:42424				
GI					



AB The present invention provides nucleoside compds. I, wherein B is nucleobase; R1 is fluoromethyl, difluoromethyl, trifluoromethyl; R2 is H, F, amino, OH, SH, alkoxy, alkylcarbonyloxy, alkyl; R3 and R4 are independently H, Cn, N3, halogen, OH, SH, amino, alkoxy, alkylcarbonyloxy, alkenyl, alkynyl; R5 is H, alkylcarbonyl, P3O9H4, P2O6H3, phosphophonyl; R6 and R7 independently H, Me, hydroxymethyl, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral

they use  
2' - CH<sub>2</sub>F, CHF<sub>2</sub>, or CF<sub>3</sub>  
molecules

infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 2-amino-9-(2-C-fluoromethyl- $\beta$ -D-ribofuranosyl)-3,9-dihydropurin-6-one was prepared and tested as inhibitor of RNA-dependent RNA viral polymerase. Title compds. tested in the HCV NS5B polymerase assay exhibited IC<sub>50</sub>'s less than 100  $\mu$ mol.

IT 510765-51-2P 636581-91-4P 636581-92-5P  
636581-93-6P 636582-01-9P 636582-02-0P  
636582-03-1P 636582-04-2P

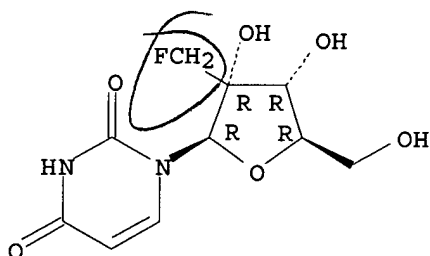
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent RNA viral polymerase)

RN 510765-51-2 CAPLUS

CN Uridine, 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

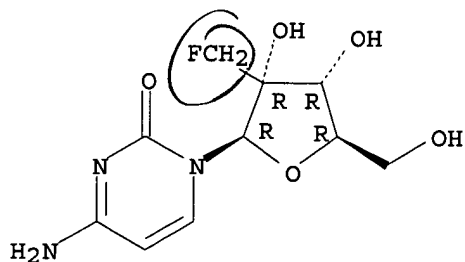
Absolute stereochemistry.



RN 636581-91-4 CAPLUS

CN Cytidine, 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

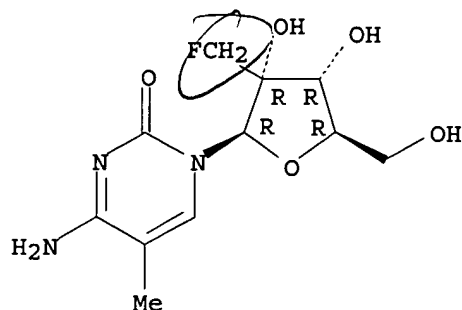


RN 636581-92-5 CAPLUS

CN Cytidine, 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

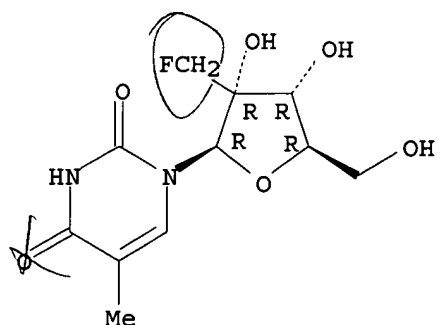
10/609,298



RN 636581-93-6 CAPLUS

CN Uridine, 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

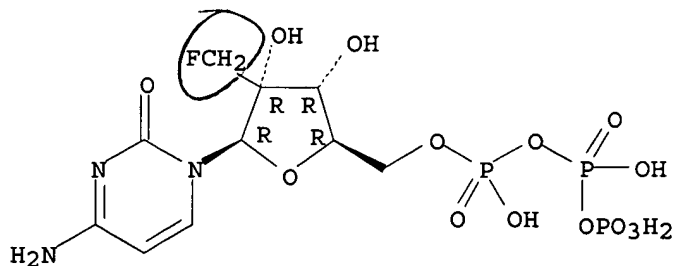
Absolute stereochemistry.



RN 636582-01-9 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

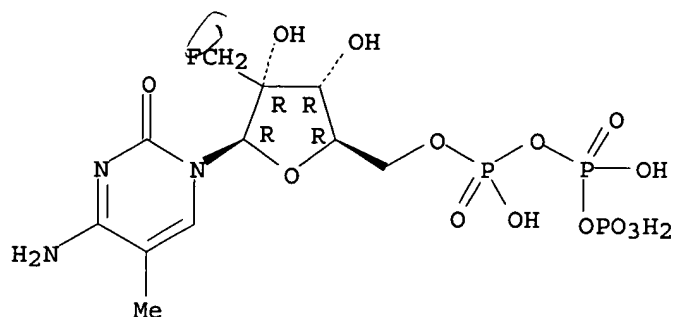


RN 636582-02-0 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

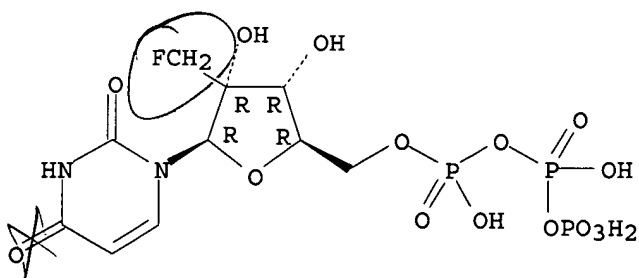
10/609,298



RN 636582-03-1 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

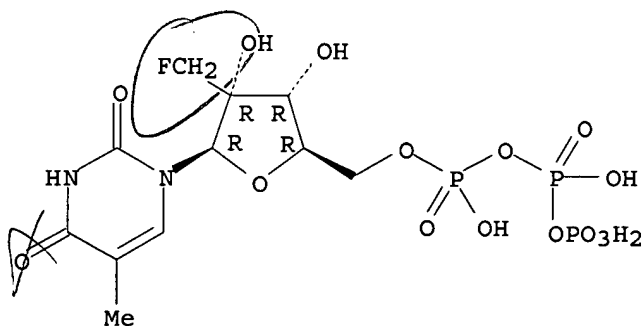
Absolute stereochemistry.



RN 636582-04-2 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:892793 CAPLUS

DN 139:365176

TI Preparation of nucleoside derivatives for treating hepatitis C virus infection

IN Roberts, Christopher Don; Dyatkina, Natalia B.; Keicher, Jesse D.; Liehr, Sebastian Johannes Reinhard; Hanson, Eric Jason

PA Genelabs Technologies, Inc., USA

SO PCT Int. Appl., 182 pp.

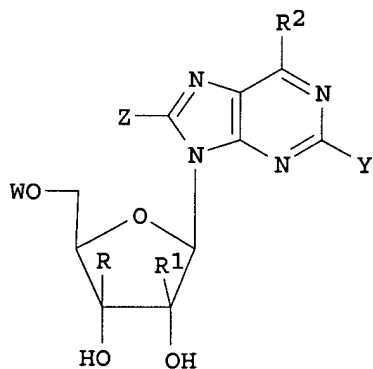
CODEN: PIXXD2

DT Patent

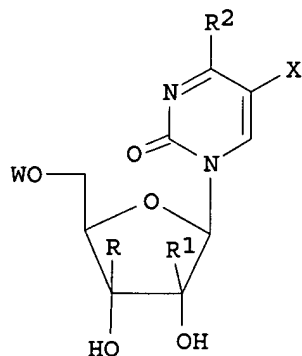
LA English

## FAN.CNT 1

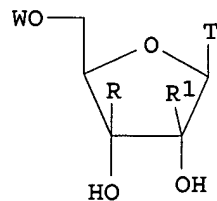
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PI	WO 2003093290	A2	20031113	WO 2003-US14237	20030506
	WO 2003093290	A3	20040318		
	WO 2003093290	C1	20050519		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	CA 2484921	AA	20031113	CA 2003-2484921	20030506
	AU 2003232071	A1	20031117	AU 2003-232071	20030506
	US 2004063658	A1	20040401	US 2003-431631	20030506
	EP 1501850	A2	20050202	EP 2003-747674	20030506
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	BR 2003009581	A	20050329	BR 2003-9581	20030506
	CN 1653077	A	20050810	CN 2003-810239	20030506
	JP 2005530759	T2	20051013	JP 2004-501429	20030506
	NO 2004005247	A	20041130	NO 2004-5247	20041130
PRAI	US 2002-378624P	P	20020506		
	US 2002-392871P	P	20020628		
	WO 2003-US14237	W	20030506		
OS	MARPAT 139:365176				
GI					



I



II



III

AB Nucleosides I-III, wherein R and R1 are independently H, alkyl, alkenyl, alkynyl, provided that R and R1 are not both H; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, acylamino, guanidino, amidino, thioacylamino, OH, alkoxy, halo, nitro, aryl, heteroaryl, substituted amine; W is H, phosphate, phosphonate, acyl, alkyl, sulfonate, lipid, amino acid, sugar residue, peptide, cholesterol; X is H, halo, alkyl, substituted amine; Y is H, halo, OH, alkylthio, substituted amine; Z is H, halo, OH, alkyl, substituted amine; T is nucleobase, were prepared as HCV RNA polymerase inhibitors and for treating hepatitis C virus infections. Thus, 2-(4-amino-pyrrolo[3,2-c]pyridin-1-yl)-5-hydroxymethyl-3-methyltetrahydro-furan-3,4-diol was prepared for treating hepatitis C virus infections (no data). Different kind of formulation such as tablet, capsule, suspension, injectable, and suppository formulation are reported.

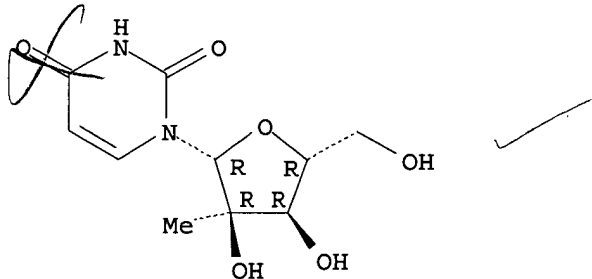
IT 31448-54-1P 119410-84-3P 622380-43-2P  
622380-45-4P 622380-47-6P 622380-48-7P  
622380-51-2P 622380-52-3P 622380-56-7P  
622380-57-8P 622380-58-9P 622380-59-0P  
622380-60-3P 622380-61-4P 622380-87-4P  
622381-09-3P 622381-10-6P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of nucleoside derivs. for treating hepatitis C virus infection)

RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

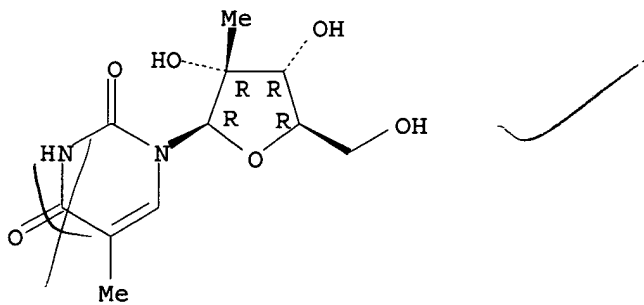
Absolute stereochemistry.



RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



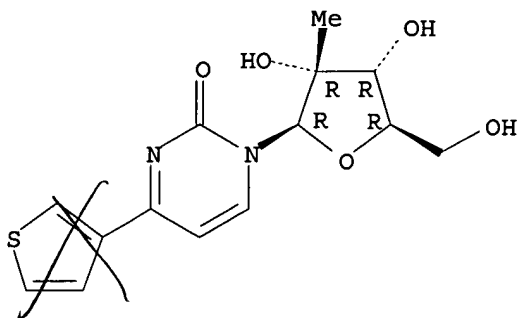
RN 622380-43-2 CAPLUS

CN 2(1H)-Pyrimidinone, 1-(2-C-methyl-β-D-ribofuranosyl)-4-(3-thienyl)-

10/609,298

(9CI) (CA INDEX NAME)

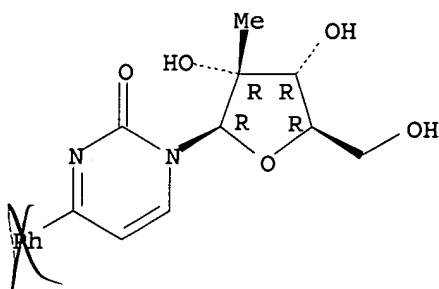
Absolute stereochemistry.



RN 622380-45-4 CAPLUS

CN 2(1H)-Pyrimidinone, 1-(2-C-methyl- $\beta$ -D-ribofuranosyl)-4-phenyl- (9CI)  
(CA INDEX NAME)

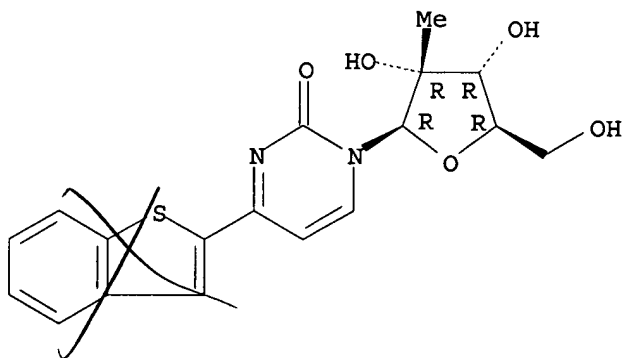
Absolute stereochemistry.



RN 622380-47-6 CAPLUS

CN 2(1H)-Pyrimidinone, 4-benzo[b]thien-2-yl-1-(2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



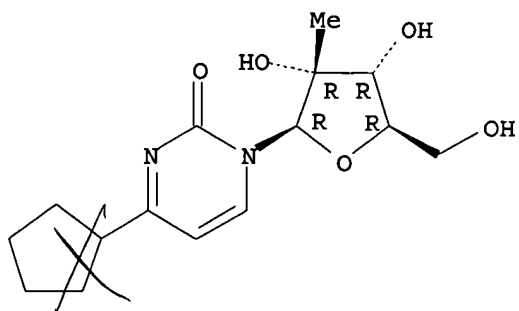
RN 622380-48-7 CAPLUS

CN 2(1H)-Pyrimidinone, 4-cyclopentyl-1-(2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



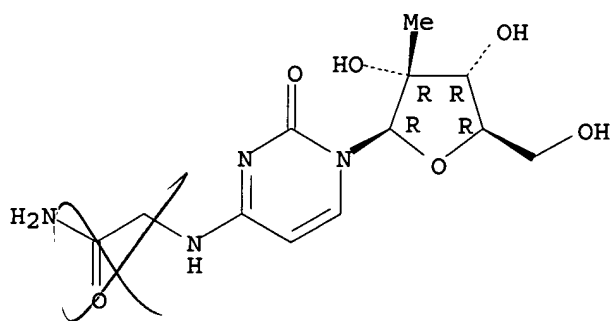
10/609,298



RN 622380-51-2 CAPLUS

CN Cytidine, N-(2-amino-2-oxoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

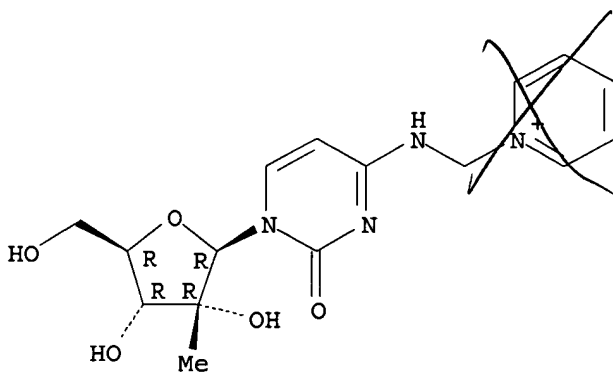
Absolute stereochemistry.



RN 622380-52-3 CAPLUS

CN Pyridinium, 1-[[[1,2-dihydro-1-(2-C-methyl-beta-D-ribofuranosyl)-2-oxo-4-pyrimidinyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

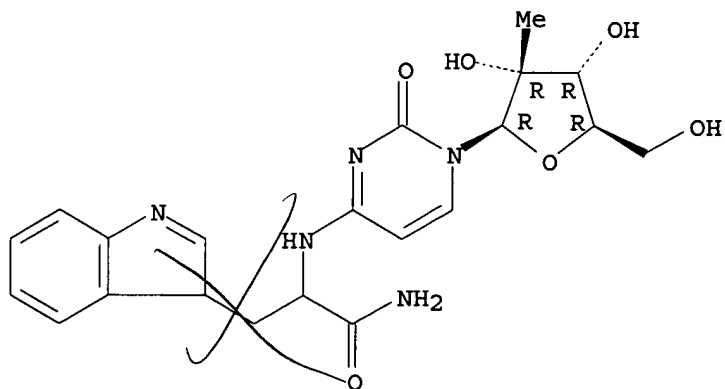


RN 622380-56-7 CAPLUS

CN Cytidine, N-[2-amino-1-(3H-indol-3-ylmethyl)-2-oxoethyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

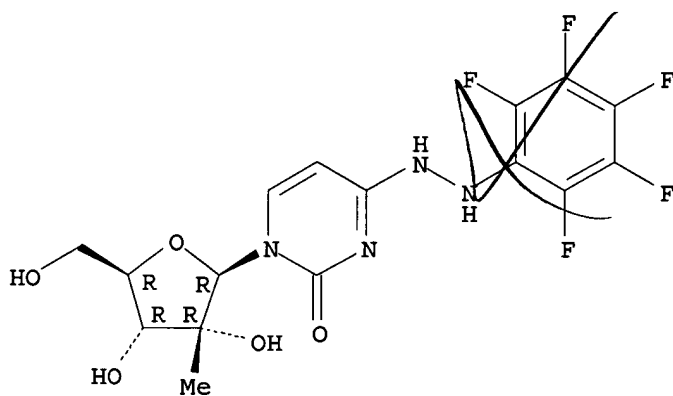
10/609,298



RN 622380-57-8 CAPLUS

CN Uridine, 2'-C-methyl-, 4-[(pentafluorophenyl)hydrazone] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

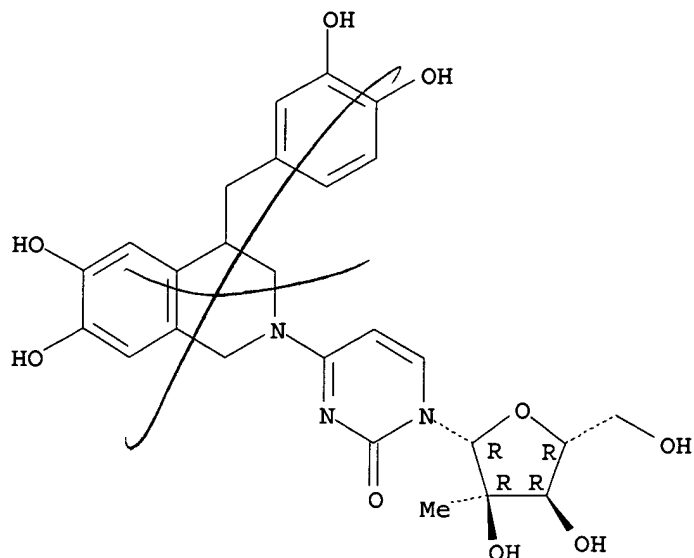


RN 622380-58-9 CAPLUS

CN 2(1H)-Pyrimidinone, 4-[4-[(3,4-dihydroxyphenyl)methyl]-3,4-dihydro-6,7-dihydroxy-2(1H)-isoquinolinyl]-1-(2-C-methyl-beta-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

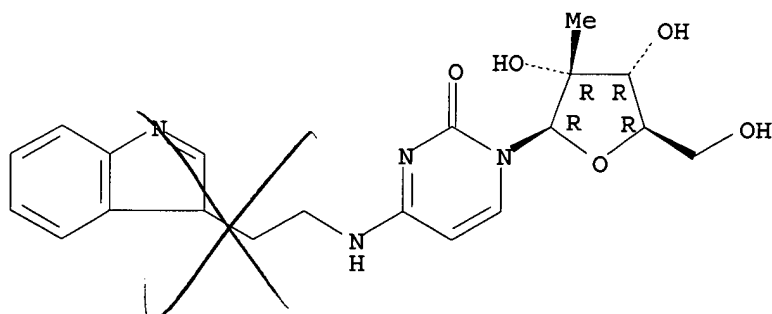
Absolute stereochemistry.

10/609,298



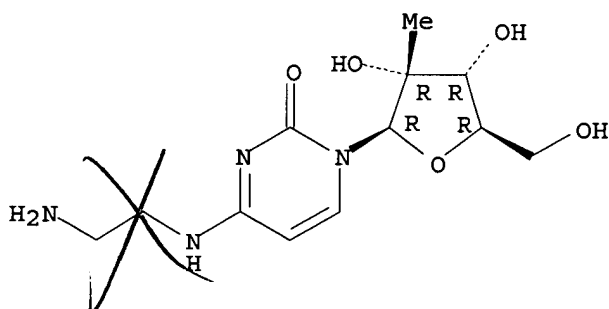
RN 622380-59-0 CAPLUS  
CN Cytidine, N-[2-(3H-indol-3-yl)ethyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 622380-60-3 CAPLUS  
CN Cytidine, N-(2-aminoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

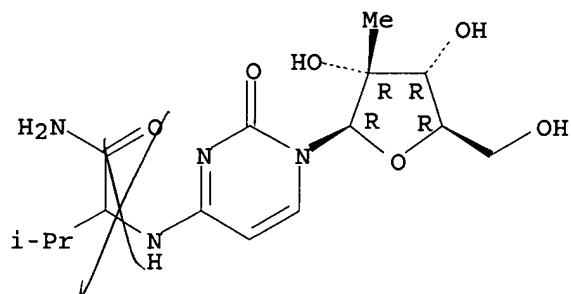
Absolute stereochemistry.



RN 622380-61-4 CAPLUS  
CN Cytidine, N-[1-(aminocarbonyl)-2-methylpropyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

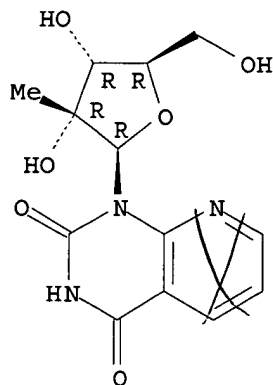
10/609,298



RN 622380-87-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione, 1-(2-C-methyl- $\beta$ -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

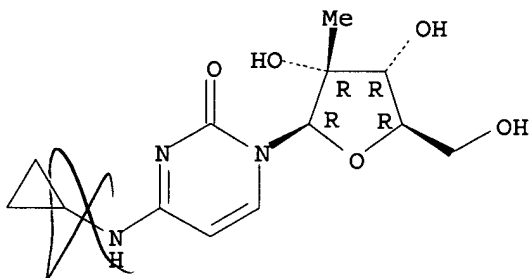
Absolute stereochemistry.



RN 622381-09-3 CAPLUS

CN Cytidine, N-cyclopropyl-2'-C-methyl- (9CI) (CA INDEX NAME)

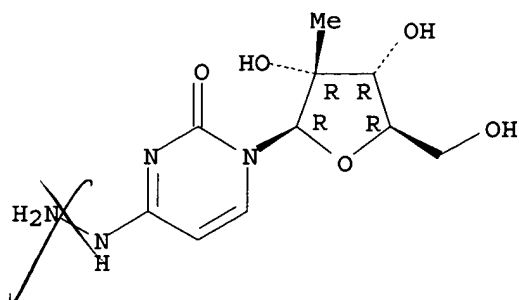
Absolute stereochemistry.



RN 622381-10-6 CAPLUS

CN Uridine, 2'-C-methyl-, 4-hydrazone (9CI) (CA INDEX NAME)

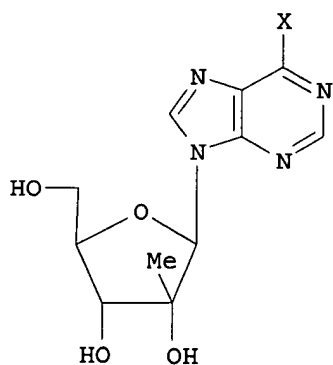
Absolute stereochemistry.



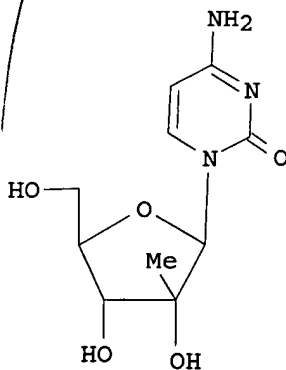
L8 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2003:591195 CAPLUS  
 DN 139:133789  
 TI Preparation of sugar modified nucleosides as antiviral agents  
 IN Hong, Zhi; An, Haoyun; Ding, Yili; Girardet, Jean-luc; Zhong, Weidong  
 PA Ribapharm Inc, USA  
 SO PCT Int. Appl., 33 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003062255	A2	20030731	WO 2002-US31556	20021002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1572705	A2	20050914	EP 2002-776103	20021002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI US 2002-350296P	P	20020117		
US 2002-391800P	P	20020626		
WO 2002-US31556	W	20021002		
OS MARPAT 139:133789				
GI				

use 4' substituted  
 not 2' substituted



I



II

AB Various 2'-modified nucleoside analogs I and II wherein X is NH<sub>2</sub>, NHMe, NMe<sub>2</sub>, OMe, SMe, and corresponding prodrugs are provided, and particularly contemplated methods of use include use as antiviral agents, and especially as antiviral agents against HCV.

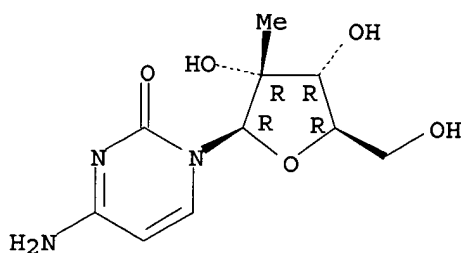
IT 20724-73-6 31448-54-1 119410-84-3  
565451-07-2 565451-08-3 565451-09-4  
565451-10-7 565451-11-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of sugar modified nucleosides as antiviral agents)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

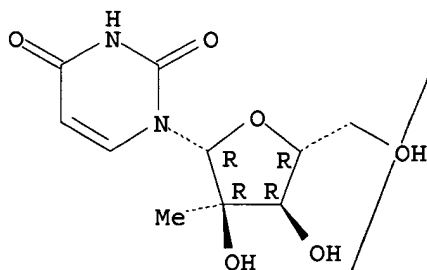
Absolute stereochemistry.



RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

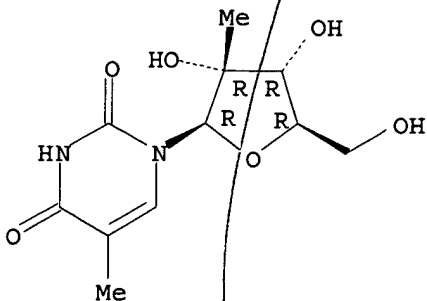
Absolute stereochemistry.



RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

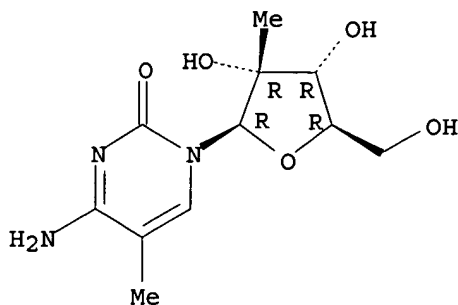


10/609,298

RN 565451-07-2 CAPLUS

CN Cytidine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

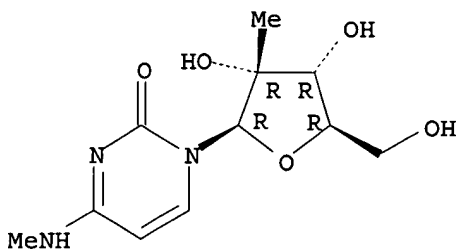
Absolute stereochemistry.



RN 565451-08-3 CAPLUS

CN Cytidine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

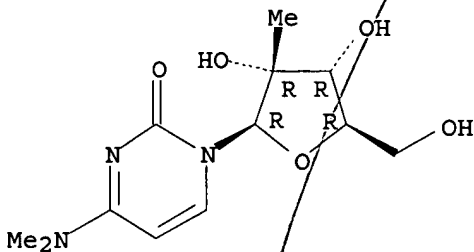
Absolute stereochemistry.



RN 565451-09-4 CAPLUS

CN Cytidine, N,N-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

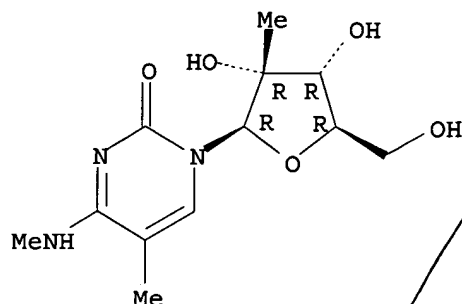


RN 565451-10-7 CAPLUS

CN Cytidine, N,5-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

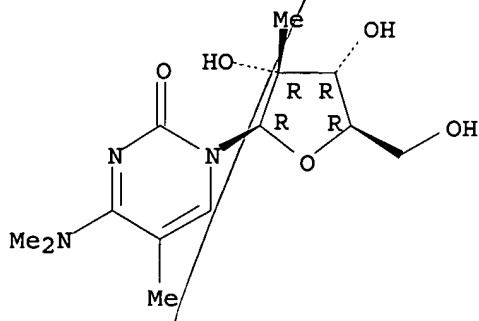
10/609,298



RN 565451-11-8 CAPLUS

CN Cytidine, N,N,5-trimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:555629 CAPLUS

DN 137:125359

TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA viral polymerase

IN Carroll, Steven S.; Lafemina, Robert L.; Hall, Dawn L.; Himmelberger, Amy L.; Kuo, Lawrence C.; Maccoss, Malcolm; Olsen, David B.; Rutkowski, Carrie A.; Tomassini, Joanne E.; An, Haoyun; Bhat, Balkrishen; Bhat, Neelima; Cook, Phillip Dan; Eldrup, Anne B.; Guinosso, Charles J.; Prhavc, Marija; Prakash, Thazha P.

PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.

SO PCT Int. Appl., 235 pp.

CODEN: PIXXD2

DT Patent

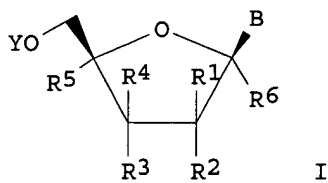
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	CA 2433878	AA	20020725	CA 2002-2433878	20020118



US 2002147160	A1	20021010	US 2002-52318	20020118
US 6777395	B2	20040817		
CN 1498221	A	20040519	CN 2002-806977	20020118
JP 2004532184	T2	20041021	JP 2002-558479	20020118
EP 1539188	A2	20050615	EP 2002-709095	20020118
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US 2004072788	A1	20040415	US 2003-431657	20030507
ZA 2003005078	A	20040521	ZA 2003-5078	20030630
US 2004067901	A1	20040408	US 2003-688691	20031017
US 2004110717	A1	20040610	US 2004-250873	20040116
US 2005272676	A1	20051208	US 2005-200499	20050809
PRAI US 2001-263313P	P	20010122		
US 2001-282069P	P	20010406		
US 2001-299320P	P	20010619		
US 2001-344528P	P	20011025		
US 2002-52318	A3	20020118		
WO 2002-US1531	W	20020118		
US 2003-431657	B1	20030507		
OS MARPAT 137:125359				
GI				



AB The present invention provides the preparation of nucleoside compds. I, wherein B is nucleobase, Y is H, alkylcarbonyl, phosphate; R1 is H, alkenyl, alkynyl, alkyl; R2 and R3 are independently H, OH, halogen, alkyl, alkoxy, alkenyloxy, alkylthio, alkylcarbonyloxy, aryloxyrcbonyl, azido, amino, alkylamino; R1 and R2 together with the carbon atom to which they are attached form a 3- to 6-membered heterocycle; R4 is H, OH, SH, NH2, alkylamino, cycloalkylamino, halogen, alkyl, alkoxy, CF3; R5 and R6 are independently H, hydroxymethyl, Me, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 4-amino-1-(2-C-methyl- $\beta$ -D-ribofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine was prepared as inhibitors of RNA-dependent RNA viral polymerase. Representative compds. tested in the HCV NS5B polymerase assay exhibited IC's less than 100  $\mu$ M. The compds. of the present invention were also evaluated for their ability to affect the replication of Hepatitis C Virus RNA in cultured hepatoma (HuH-7) cells containing a sub-genomic HCV Replicon.

IT 20724-73-6P 114262-49-6P 374750-28-4P  
444019-82-3P 444020-83-1P 444022-03-1P

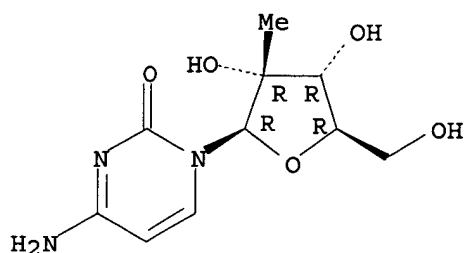
10/609,298

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA viral polymerase)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

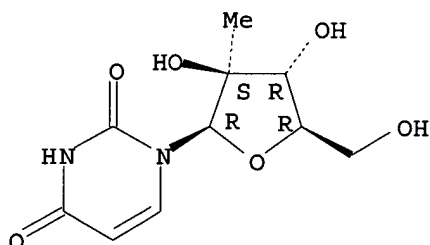
Absolute stereochemistry.



RN 114262-49-6 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-C-methyl-β-D-arabinofuranosyl)- (9CI) (CA INDEX NAME)

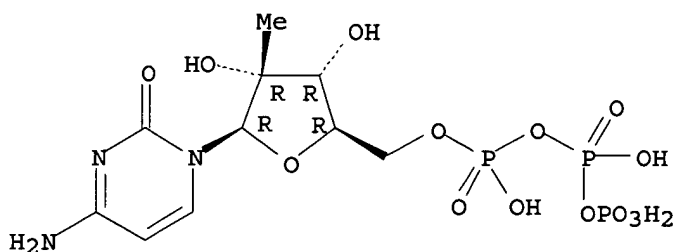
Absolute stereochemistry.



RN 374750-28-4 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

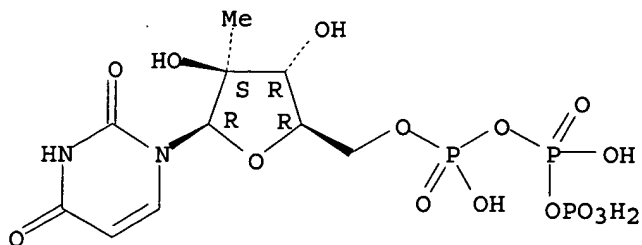


RN 444019-82-3 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-2-C-methyl-β-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

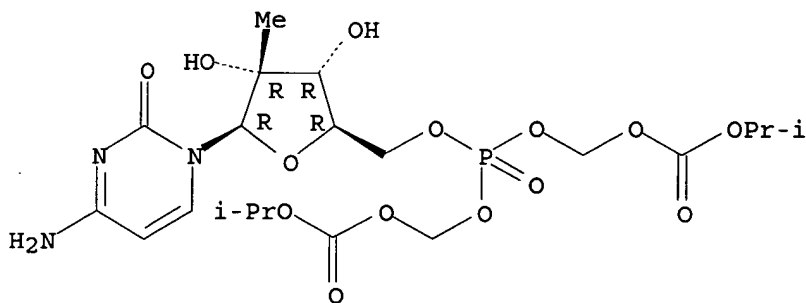
10/609,298



RN 444020-83-1 CAPLUS

CN 5'-Cytidylic acid, 2'-C-methyl-, bis[[[(1-methylethoxy)carbonyl]oxy]methyl]  
] ester (9CI) (CA INDEX NAME)

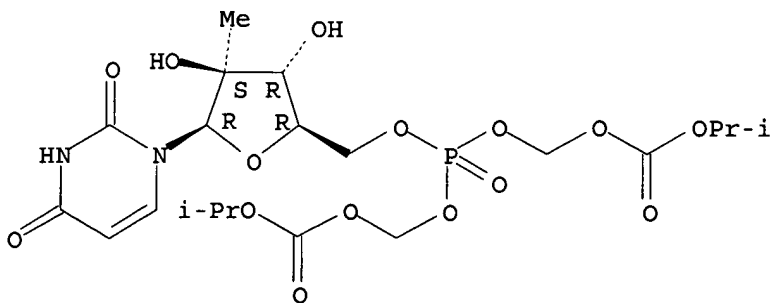
Absolute stereochemistry.



RN 444022-03-1 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-C-methyl-5-O-[7-methyl-1-[[[(1-methylethoxy)carbonyl]oxy]methoxy]-1-oxido-5-oxo-2,4,6-trioxa-1-phosphaoct-1-yl]-β-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:886155 CAPLUS

DN 136:590

TI Methods and compositions using modified nucleosides for treating  
flaviviruses and pestiviruses

IN Sommadossi, Jean-Pierre; Lacolla, Paolo

PA Novirio Pharmaceuticals Limited, Cayman I.; Universita Degli Studi Di  
Cagliari

SO PCT Int. Appl., 302 pp.

CODEN: PIXXD2

DT Patent

10/609,298

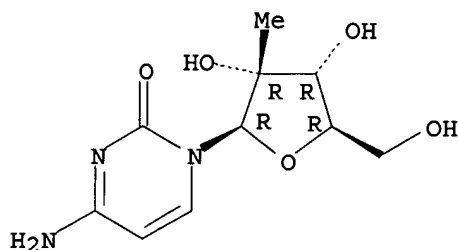
LA English  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001092282	A2	20011206	WO 2001-US16687	20010523
	WO 2001092282	A3	20020502		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2410579	AA	20011206	CA 2001-2410579	20010523
	EP 1294735	A2	20030326	EP 2001-952131	20010523
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003060400	A1	20030327	US 2001-863816	20010523
	US 6812219	B2	20041102		
	BR 2001011196	A	20040406	BR 2001-11196	20010523
	JP 2004510698	T2	20040408	JP 2002-500895	20010523
	NO 2002005600	A	20030117	NO 2002-5600	20021121
	ZA 2002010112	A	20040623	ZA 2002-10112	20021212
	US 2004063622	A1	20040401	US 2003-602693	20030620
	US 2004097462	A1	20040520	US 2003-602692	20030620
	US 2004102414	A1	20040527	US 2003-602694	20030620
PRAI	US 2000-207674P	P	20000526		
	US 2001-283276P	P	20010411		
	US 2001-863816	A3	20010523		
	WO 2001-US16687	W	20010523		
OS	MARPAT 136:590				
AB	A method and composition are provided for treating a host infected with flavivirus or pestivirus, comprising administering an effective amount of a 1', 2' or 3'-modified nucleoside or a pharmaceutically acceptable salt or prodrug thereof.				
IT	20724-73-6 31448-54-1 119410-84-3				
	RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleoside derivs. for treating flaviviruses and pestiviruses)				
RN	20724-73-6 CAPLUS				
CN	Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)				

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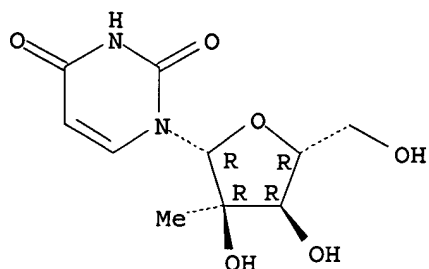
Absolute stereochemistry.



RN 31448-54-1 CAPLUS  
CN Uridine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

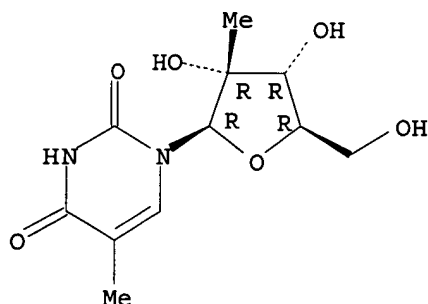
10/609,298



RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



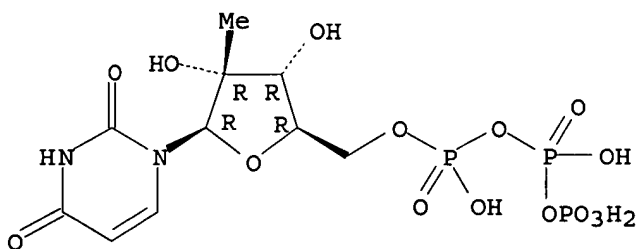
IT 125911-76-4 374750-28-4

RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)  
(nucleoside derivs. for treating flaviviruses and pestiviruses)

RN 125911-76-4 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

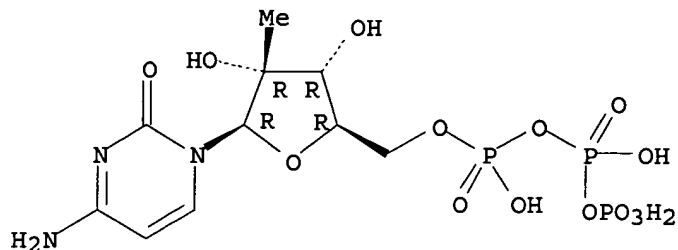
Absolute stereochemistry.



RN 374750-28-4 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

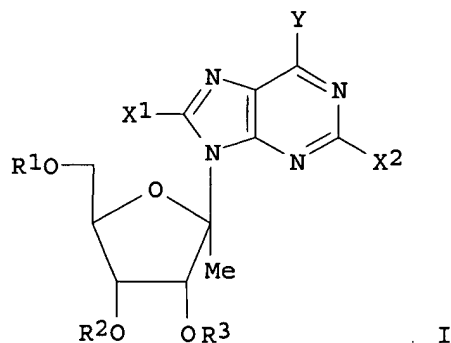


L8 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2001:868467 CAPLUS  
 DN 136:6296  
 TI Preparation of antiviral nucleosides and methods for treating  
 hepatitis C virus  
 IN Sommadossi, Jean-Pierre, Lacolla, Paulo  
 PA Novirio Pharmaceuticals Limited, Cayman I.; Universita degli Studi di  
 Cagliari  
 SO PCT Int. Appl., 296 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

*Do O'DP*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001090121	A2	20011129	WO 2001-US16671	20010523
WO 2001090121	A3	20020502		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2409613	AA	20011129	CA 2001-2409613	20010523
AU 2001074906	A5	20011203	AU 2001-74906	20010523
US 2003050229	A1	20030313	US 2001-864078	20010523
US 6914054	B2	20050705		
EP 1292603	A2	20030319	EP 2001-941564	20010523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011127	A	20030624	BR 2001-11127	20010523
JP 2004533401	T2	20041104	JP 2001-586308	20010523
NZ 522863	A	20050729	NZ 2001-522863	20010523
EP 1669364	A2	20060614	EP 2006-75216	20010523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO, CY, TR				
NO 2002005627	A	20030106	NO 2002-5627	20021122
ZA 2002010101	A	20040614	ZA 2002-10101	20021212
US 2004097461	A1	20040520	US 2003-602691	20030620
US 2004101535	A1	20040527	US 2003-602976	20030620
US 2005124532	A1	20050609	US 2003-602142	20030620
US 2005137161	A1	20050623	US 2003-602136	20030620
PRAI US 2000-206585P	P	20000523		
EP 2001-941564	A3	20010523		
US 2001-864078	A1	20010523		
WO 2001-US16671	W	20010523		
OS MARPAT 136:6296				

GI



AB A method and composition for treating a host infected with hepatitis C comprising administering an effective hepatitis C treatment amount of a described 1'-, 2'- or 3'-modified nucleosides I, wherein : R1-R3 and R are independently H, phosphate (including mono, di- or triphosphate and a stabilized phosphate prodrug); acyl; alkyl; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered in vivo is capable of providing a compound wherein R1-R3 are independently H or phosphate; Y is hydrogen, bromo, chloro, fluoro, iodo, OR4, NR4R5 or SR4; X1 and X2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR4, NR4R5 or SR4; and R4 and R5 are independently hydrogen, acyl, alkyl or a pharmaceutically acceptable salt or prodrug thereof, is provided. Thus, I (R1-R3 = X1 = X2 = H, Y = NH2) was prepared and tested in Cynomolgus monkeys as antiviral agent. Oral bioavailability in monkeys, bone human bone marrow toxicity (IC50 > 10  $\mu$ M), and mitochondrial toxicity, were reported .

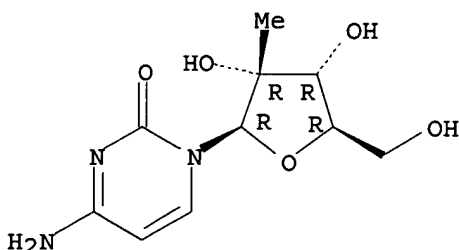
IT 20724-73-6P 31448-54-1P 119410-84-3P  
125911-76-4P 374750-28-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of antiviral nucleosides and methods for treating hepatitis C virus)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

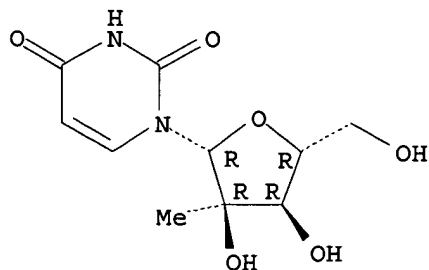


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RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

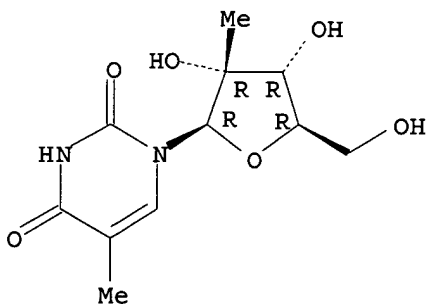
Absolute stereochemistry.



RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

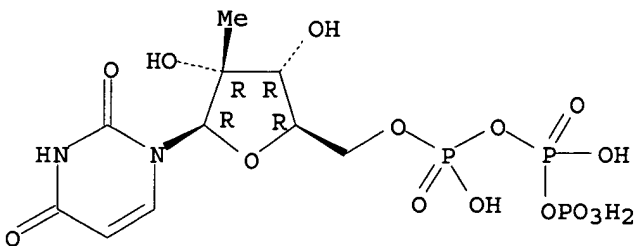
Absolute stereochemistry.



RN 125911-76-4 CAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 374750-28-4 CAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/609,298

